

UNIVERSITA' VITA-SALUTE SAN RAFFAELE

**CORSO DI DOTTORATO DI RICERCA
IN SCIENZE COGNITIVE E COMPORTAMENTALI**

**UNCOVERING DATA-DRIVEN
SUBTYPES OF DEPRESSION BASED
ON NEUROBIOLOGICAL AND
ENVIRONMENTAL SIGNATURES:
A MACHINE LEARNING APPROACH**

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Matr. 021923

Ciclo di dottorato XXXVIII

SSD MED/25

Anno Accademico 2024/2025

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CONSULTAZIONE TESI DI DOTTORATO DI RICERCA

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ACKNOWLEDGEMENTS

The execution of this thesis was made possible through the support of several institutions. Financial support was provided by Vita-Salute San Raffaele University (Milan, Italy), which awarded a doctoral scholarship. Logistical and resource support were supplied by the Unit of Psychiatry and Clinical Psychobiology, Division of Neuroscience, IRCCS Ospedale San Raffaele (Milan, Italy), which gave me the necessary means for the project. Additional funding was secured from the Italian Ministry of Health (Grant Number GR-2019-12370616). Research activities involving the UK Biobank were conducted under Application Number 56514, “Stratification of health outcomes in mood disorders”.

SOMMARIO

I disturbi dell'umore sono clinicamente e biologicamente eterogenei, con pazienti che esibiscono differenze significative nei profili sintomatici, decorso clinico, neurobiologia sottostante, predisposizione genetica ed esposizione ambientale. Questa eterogeneità ha ostacolato l'identificazione di biomarcatori affidabili e limitato l'efficacia dei trattamenti. Recenti tentativi di stratificazione hanno utilizzato approcci unimodali, senza validazione esterna. Pertanto, sfruttando i progressi della psichiatria computazionale, questo progetto mirava a (i) identificare sottotipi di depressione robusti, replicabili, biologicamente e clinicamente significativi con un approccio multimodale e (ii) valutarne l'utilità clinica e predittiva. Abbiamo combinato tecniche di *machine learning* supervisionato e non, su due grandi coorti – un campione con disturbo depressivo maggiore (MDD) proveniente dalla UK Biobank (n=3887) e un campione clinico di pazienti con MDD e disturbo bipolare (BD) ricoverati presso l'IRCCS Ospedale San Raffaele (n=475) – utilizzando neuroimaging multimodale (i.e., MRI strutturale, di diffusione, funzionale a riposo e durante compiti), punteggi poligenici e dati relativi allo stress. Attraverso un approccio di *consensus clustering*, abbiamo identificato due biotipi riproducibili. Uno dei due, in linea con un sottotipo “immuno-metabolico”, ha mostrato alterazioni strutturali e funzionali diffuse (i.e., ridotti spessore e volume corticale, integrità della sostanza bianca, connettività e attivazione funzionale), aumentato rischio poligenico per marcatori infiammatori (e.g., MIF e RANTES), maggiore comorbidità cardiometabolica e minore velocità di elaborazione e motoria rispetto all'altro. I modelli supervisionati che predicono l'appartenenza al cluster hanno supportato la validità esterna di questi sottotipi con elevata accuratezza, mentre i modelli che predicono caratteristiche cliniche in ciascun sottotipo (e.g., resistenza al trattamento, comorbidità somatiche e gesti autolesivi) hanno evidenziato possibili differenze patofisiologiche tra biotipi e un diverso contributo delle specifiche modalità: per esempio, le misure di diffusività hanno contribuito di più alla previsione del rischio cardiovascolare in tutte le coorti, mentre l'attivazione emotiva è stata la più informativa per la resistenza al trattamento negli stati acuti di malattia. In conclusione, il presente studio va oltre la nosologia psichiatrica basata sui sintomi verso una stratificazione della depressione informata neurobiologicamente, ed evidenzia la necessità di un approccio psichiatrico di precisione in cui le strategie di prevenzione e trattamento possano essere adattate ai correlati biologici sottostanti al sottotipo.

ABSTRACT

Mood disorders are clinically and biologically heterogeneous, with patients significantly differing in symptom profiles, clinical course, underlying neurobiology, genetic liability, and environmental exposures. This heterogeneity has long hampered the identification of reliable biomarkers and limited treatment efficacy. Recent attempts to stratify patients based on shared characteristics employed single-modality approaches and lacked external validation. Therefore, by leveraging advances in computational psychiatry, this project aimed to (i) identify robust, replicable, biologically and clinically meaningful subtypes of depression from multiple features and (ii) evaluate their clinical and predictive utility. We combined unsupervised and supervised machine learning in two large cohorts – a lifetime major depressive disorder (MDD) sample from UK Biobank (n=3,887) and a clinical inpatient sample including currently depressed MDD and bipolar disorder (BD) patients from IRCCS Ospedale San Raffaele (n=475) – using multimodal neuroimaging (i.e., structural MRI, diffusion MRI, resting-state and task fMRI), polygenic scores, and stress-related data. Through a consensus clustering approach, we identified two reproducible biotypes across settings, illness states, and diagnoses. One subtype, converging with an “immune-metabolic” phenotype of depression, showed widespread structural and functional alterations (i.e., reduced cortical thickness and volume, lower white-matter integrity, weaker resting-state connectivity, and functional hypoactivation), heightened polygenic risk for inflammatory markers (e.g., MIF and RANTES), higher cardio-metabolic comorbidity, and poorer processing and motor speed with respect to the other. Supervised elastic-net models predicting cluster membership supported the external validity of these subtypes with high accuracy, while models predicting health outcomes in each subtype (e.g., treatment resistance, somatic comorbidities, and self-harm) highlighted differential pathophysiological pathways within biotypes and complementary modality contributions to risk: for instance, diffusivity measures were the strongest contributors to cardiovascular risk prediction across cohorts, whereas task-evoked emotional activation was most informative for treatment-resistance during acute states of the illness. In conclusion, the current study moves beyond symptom-based psychiatric nosology towards a neurobiologically-informed stratification of depression, and highlights the need for a precision psychiatry approach where prevention and treatment strategies might be tailored to the subtype's underlying biological correlates.

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ACRONYMS AND ABBREVIATIONS

ACC: Anterior cingulate cortex
ACE: Adverse childhood experience
AD: Axial diffusivity
ADHD: Attention-deficit/hyperactivity disorder
ALFF: Amplitude of low-frequency fluctuations
AN: Anorexia nervosa
AUC: Area under the receiver operator curve
BA: Balanced accuracy
BACS: Brief Assessment of Cognition in Schizophrenia
BBR: Boundary-based registration
BD: Bipolar disorder
BDI: Beck Depression Inventory
BDNF: Brain-derived neurotrophic factor
BET: Brain extraction tool
BMI: Body mass index
bNGF: Beta nerve growth factor
BOLD: Blood oxygenation level dependent
CAD: Coronary artery disease
CBT: Cognitive behavioral therapy
CCL: C-C motif ligand
CES-D: Center for Epidemiologic Studies Depression Scale
CI: Confidence interval
CIDI-SF: Composite International Diagnostic Interview, Short Form
Cl: Cluster
CPT: Conners' Continuous Performance Test
CRP: C-reactive protein
CSF: Colony-stimulating factor
CTACK: Cutaneous T-cell attracting chemokine
CTQ: Childhood Trauma Questionnaire
CTS-5: Childhood Trauma Screener
CUD: Cannabis use disorder

CXCL: C motif chemokine ligand
DAN: Dorsal attention network
DB: Davies-Bouldin index
DBSCAN: Density-Based Spatial Clustering of Applications with Noise
dlPFC: Dorsolateral prefrontal cortex
dMDD: Depressed individuals with lifetime MDD
DMN: Default mode network
DNA: Deoxyribonucleic acid
DSM: Diagnostic and Statistical Manual of Mental Disorders
DTI: Diffusion tensor imaging
ECT: Electroconvulsive therapy
ELS: Early life stress
ENIGMA: Enhancing Neuro Imaging Genetics through Meta-Analysis
EPI: Echo-planar imaging
FA: Fractional anisotropy
fALFF: Fractional amplitude of low-frequency fluctuations
FAST: FMRIB's Automated Segmentation Tool
FC: Functional connectivity
FDR: False discovery rate
FEAT: FMRIB's Expert Analysis Tool
FGFb: Basic fibroblast growth factor
FIRST: FMRIB's Integrated Registration and Segmentation Tool
FLIRT: FMRIB's Linear Image Registration Tool
fMRI: Functional magnetic resonance imaging
FNIRT: FMRIB's Nonlinear Image Registration Tool
FOV: Field of view
FPN: Frontoparietal network
FSL: FMRIB's Software Library
GBD: Global Burden of Diseases
GDC: Gradient distortion correction
GIMME: Group iterative multiple model estimation
GLM: General linear model

GM: grey matter
GMM: Gaussian mixture model
GPRS: Genomic profile risk score
GWAS: Genome-wide association study
GxE: Gene-environment interaction
HADS: Hospital Anxiety and Depression Scale
HAM-D: Hamilton Depression Rating Scale
HCP: Human Connectome Project
HDL: High-density lipoprotein
HGF: Hepatocyte growth factor
HiTOP: Hierarchical Taxonomy of Psychopathology
HPA: Hypothalamic-pituitary-adrenal
HR: Hazard ratio
HRC: Haplotype Reference Consortium
IC: Independent component
ICA: Independent component analysis
ICD: International Classification of Diseases
IDP: Imaging-derived phenotype
IFN γ : Interferon-gamma
IL: Interleukin
IL1RA: Interleukin-1 receptor antagonist
IL2RA: Interleukin-2 receptor, alpha subunit
IPT: Interpersonal therapy
iSPOT-D: International Study to Predict Optimized Treatment in Depression
JHU: Johns Hopkins University
LCA: Latent class analysis
LD: Linkage disequilibrium
LDL: Low-density lipoprotein
LPA: Latent profile analysis
MADRS: Montgomery-Åsberg Depression Rating Scale
MB: Multiband
MD: Median diffusivity

MDD: Major depressive disorder
MIF: Macrophage migration inhibitory factor
ML: Machine learning
MNI: Montreal Neurological Institute
MRI: Magnetic resonance imaging
NA: Not applicable
NESARC: National Epidemiologic Survey on Alcohol and Related Conditions
NESDA: Netherlands Study of Depression and Anxiety
NS: Not significant
OCD: Obsessive-compulsive disorder
OFC: Orbitofrontal cortex
OR: Odds ratio
OSR: IRCSS Ospedale San Raffaele
PCA: Principal component analysis
PCC: Posterior cingulate cortex
PDGFbb: Platelet derived growth factor BB
PFC: Prefrontal cortex
PGC: Psychiatric Genomics Consortium
PGS: Polygenic score
PHQ-9: Patient Health Questionnaire-9
PTSD: Post-traumatic stress disorder
QC: Quality control
QIDS: Quick Inventory of Depressive Symptomatology
RANTES: Regulated on activation, normal T-cell expressed and secreted
RAP: Research Analysis Platform
RD: Radial diffusivity
RDoC: Research Domain Criteria
RDS-4: Recent Depressive Symptoms
ReHo: Regional homogeneity
rMDD: Remitted major depressive disorder
RNA: Ribonucleic acid
ROI: Region of interest

RR: Risk ratio

rsFC: Resting-state functional connectivity

rs-fMRI: Resting-state functional magnetic resonance imaging

SCF: Stem cell factor

SCGFb: Stem cell growth factor beta

SCID: Structured Clinical Interview for the Diagnosis of DSM-5 Disorders

SCZ: Schizophrenia

SD: Standard deviation

SE-EPI: Spin-echo echo-planar imaging

Sil: Silhouette score

SLE: Stressful life event

SMN: Somatomotor network

SN: Salience network

Sneg: Strength of negative resting-state connections

SNP: Single-nucleotide polymorphism

SNRI: Serotonin-norepinephrine reuptake inhibitor

Spos: Strength of positive resting-state connections

SRE: Schedule of Recent Experiences

SSRI: Selective serotonin reuptake inhibitor

STG: Superior temporal gyrus

T2D: Type 2 diabetes

TBSS: Tract-Based Spatial Statistics

TE: Echo time

t-fMRI: Task-based functional magnetic resonance imaging

TI: Inversion time

TMS: Transcranial magnetic stimulation

TNF: Tumor necrosis factor

TR: Repetition time

TRAIL: TNF-related apoptosis inducing ligand

TRD: Treatment-resistant depression

UKB: UK Biobank

UMAP: Uniform manifold approximation and projection

VEGF: Vascular endothelial growth factor

VIP: Variable inclusion probability

VIS: Visual network

vmPFC: Ventromedial prefrontal cortex

WES: Whole exome sequencing

WGS: Whole genome sequencing

WHO: World Health Organization

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1. Introduction

1.1 Mood disorders

Mood disorders are pervasive and debilitating psychiatric conditions primarily characterized by significant alterations in emotional states, often leading to long-lasting functional impairment and a reduced quality of life (American Psychiatric Association, 2022; World Health Organization, 2023). These disorders encompass a wide range of conditions, including depressive disorders and bipolar disorders, which involve episodes of both depression and mania or hypomania. The global burden of mood disorders is continuously growing, making them a leading cause of disability worldwide. Indeed, the World Health Organization (WHO) estimates that depression affects over 280 million people globally, with a lifetime prevalence of nearly 5%, thereby contributing significantly to the social and economic burden of disease and imposing substantial healthcare costs (GBD 2019 Mental Disorders Collaborators, 2022; World Health Organization, 2023).

Current diagnostic frameworks, such as the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR) and the International Classification of Diseases, Eleventh Revision (ICD-11), primarily rely on symptom-based criteria to define and classify mood disorders (American Psychiatric Association, 2022; World Health Organization, 2019). While these categorical systems facilitate communication among clinicians and researchers, they have been increasingly recognized for their limitations in capturing the underlying biological heterogeneity and complex clinical presentations observed in affected individuals (Cuthbert & Insel, 2013; Insel et al., 2010). Therefore, the following sections will describe the primary characteristics of main mood disorders (i.e., Major Depressive Disorder and Bipolar Disorder) as defined by contemporary diagnostic classification systems, exploring the key insights generated through the application of these diagnostic frameworks, alongside a critical examination of the significant challenges and limitations arising from such symptom-based classifications.

1.1.1 Major Depressive Disorder

Major Depressive Disorder (MDD) is a severe and persistent mood disorder characterized by several emotional, cognitive, and somatic symptoms that significantly impair daily psychosocial functioning. According to the DSM-5-TR, MDD is characterized by one or more depressive episodes separated by periods of remission. A core diagnostic criterion for an MDD episode is the presence of either a persistently depressed mood or a significant loss of interest or pleasure (i.e., anhedonia) for at least two weeks. Specifically, an MDD diagnosis requires the concurrent presence of five or more characteristic symptoms within the same two-week period, representing a notable deviation from an individual's prior functioning (American Psychiatric Association, 2022). At least one of these symptoms must be either depressed mood or anhedonia, while the additional symptoms for an MDD diagnosis encompass significant alterations in appetite or weight, disturbances in sleep (i.e., insomnia or hypersomnia), psychomotor agitation or retardation, pervasive fatigue or loss of energy, feelings of worthlessness or excessive guilt, impaired cognitive function (i.e., diminished ability to think, make decisions, or concentrate), and recurrent thoughts of death or suicidal ideation (Malhi & Mann, 2018).

Epidemiologically, MDD is highly prevalent, with lifetime prevalence rates estimated to be approximately 10% in the general population, and a 12-month prevalence of 4–5% worldwide (GBD 2019 Mental Disorders Collaborators, 2022). Although its onset can occur at any age, the first episode usually takes place in early adulthood, with a median age of onset around 25 years (Herrman et al., 2022), and affects women at nearly twice the rate of men (Salk et al., 2017).

The typical trajectory of depressive episodes varies significantly between community settings and clinical populations. Indeed, in community-based surveys, the median duration of a depressive episode is typically 2-6 months, with over 70% of these episodes resolving within 12 months, often leading to sustained remission (Ten Have et al., 2017). Conversely, studies conducted in primary and secondary mental healthcare settings reveal that 34% to 48% of patients experience persistent episodes extending beyond 12 months, with rates of recurrence reaching up to 85%, and many patients experiencing only partial remission between episodes (Herrman et al., 2022).

Despite the availability of various treatment modalities, including antidepressant medications (e.g., selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs)), psychotherapy (e.g., cognitive behavioral therapy (CBT), interpersonal therapy (IPT)), and neuromodulation techniques (e.g., transcranial magnetic stimulation (TMS), electroconvulsive therapy (ECT)), a great proportion of MDD patients do not adequately respond to first-line treatments (Dodd et al., 2021; Pérez-Sola et al., 2021). Moreover, up to 30% of patients fail multiple antidepressant interventions, resulting in what is described as treatment-resistant depression (TRD) (McIntyre et al., 2023).

The public health burden of MDD is further complicated by its high associated risk of mortality. This increased mortality is largely attributable to the elevated rates of comorbid physical diseases observed in individuals with MDD compared to the general population, including diabetes, obesity, cardiovascular diseases, dementia, and substance use disorders (Berk et al., 2023; GBD 2019 Mental Disorders Collaborators, 2022; Weir & Rapaport, 2022). For instance, meta-analytic evidence suggests that MDD patients have an increased risk of developing subsequent ischemic heart disease and stroke, with hazard ratios of 1.63 (95% CI: 1.36-1.95) and 1.94 (95% CI: 1.63-2.30), respectively (Wium-Andersen et al., 2020). Similarly, the risk of having comorbid type 2 diabetes (T2D) or metabolic syndrome is 1.18 (95% CI: 1.12–1.24) and 1.38 (95% CI: 1.17–1.64) times higher, respectively (Graham et al., 2020; Moradi et al., 2021). Furthermore, suicide stands as a critical factor in increasing mortality, with MDD being a leading cause of death worldwide. Indeed, a diagnosis of MDD heightens the risk of death by suicide by nearly 20 times compared to individuals without the disorder (Serra et al., 2022).

1.1.2 Bipolar Disorder

Bipolar Disorder (BD) is a chronic and recurrent mood disorder characterized by severe fluctuations in mood and energy, with alternating episodes of elevated or irritable mood (i.e., mania or hypomania) and depressive episodes. These mood disruptions lead to substantial impairments across cognitive, social, and occupational domains (American Psychiatric Association, 2022). As defined by the DSM-5-TR, BD can be classified into two distinct subtypes: Bipolar I Disorder (BD-I) and Bipolar II Disorder (BD-II). BD-I is diagnosed when an individual has experienced at least one episode of mania. A manic

episode is characterized by a period of abnormally and persistently elevated, expansive, or irritable mood and abnormally and persistently increased activity or energy, lasting at least one week and present for most of the day, nearly every day, or any duration if hospitalization is necessary (American Psychiatric Association, 2022). While depressive episodes are frequently observed in BD-I patients, they do not represent a diagnostic requirement, as 1-3% of patients with BD-I may present with unipolar mania (Stokes et al., 2020). In contrast, a diagnosis of BD-II needs the occurrence of at least one hypomanic episode preceded or followed by at least one major depressive episode (American Psychiatric Association, 2022). Hypomania represents a less severe form of mania, typically not accompanied by significant social or occupational dysfunction, nor requiring hospitalization. Remarkably, depressive episodes are the predominant feature in BD-II, posing significant diagnostic challenges in differentiating it from MDD. Nevertheless, some clinical indicators of bipolar depression exist and may support the diagnostic process, including atypical symptoms such as hypersomnia and hyperphagia, the presence of psychotic features, frequent mood episodes, high rates of psychiatric comorbidities, and a family history of psychiatric disorders (McIntyre et al., 2020).

Epidemiological studies suggest that the lifetime prevalence of BD ranges from 1% to 2.5% globally, with similar rates across sexes and ethnicities (Grande et al., 2016; Rowland & Marwaha, 2018), and a typical age of onset between the ages of 15 and 25 (Nierenberg et al., 2023). Early-onset BD, particularly during childhood or adolescence, is often linked to poorer prognosis, as these patients tend to have higher rates of psychiatric comorbidities, such as substance abuse, anxiety disorders, more severe mood symptoms, and longer treatment delays (Joslyn et al., 2016; Treuer & Tohen, 2010). Despite these early indicators, the diagnosis of BD is frequently delayed by 5 to 10 years (Kalman et al., 2021), with a pooled mean of 5.8 years intercurring between the disorder's onset and its management (Dagani et al., 2017).

The clinical course, diagnostic accuracy, and prognosis of BD are further hindered by high rates of comorbid psychiatric and medical conditions, whose prevalence is estimated to be approximately 90% (Merikangas et al., 2007). In particular, anxiety disorders and substance abuse are the most prevalent among psychiatric comorbidities, affecting more than 70% of individuals with BD (McIntyre et al., 2020). Additionally, various medical conditions, including circulatory, respiratory, and digestive system

diseases, as well as endocrine and metabolic disorders, are observed in 8% to 36% of BD patients (Onyeka et al., 2019; Wang et al., 2022).

The presence of physical comorbidities in BD is associated with a more severe disease trajectory, including earlier age of onset, increased risk of suicide, lower response rates, as well as premature mortality (McIntyre et al., 2020). Indeed, meta-analytic evidence suggests that individuals with BD have a reduced life expectancy of 12 to 14 years, with a 2-fold increase in mortality compared to the general population (Hayes et al., 2015). Cardiovascular diseases, in particular, are the leading cause of mortality in BD, with a 1.73-fold higher cardiovascular mortality occurring on average 17 years earlier than the general population (Nierenberg et al., 2023). Beyond physical health, suicidality also contributes to the heightened mortality rates in BD. Indeed, individuals diagnosed with BD exhibit a 20- to 30-fold increased risk of suicide compared to the general population (Pompili et al., 2013), with 30-50% of adults with BD attempting suicide at least once during their lifetime, and 15-20% of BD patients completing suicide (Miller & Black, 2020; Schaffer et al., 2015).

1.2 Heterogeneity in mood disorders

Despite the widespread clinical recognition and public health burden of mood disorders, underscoring the urgent need for enhanced diagnostic procedures and clinical management strategies, a significant challenge in clinical practice lies in their profound heterogeneity (American Psychiatric Association, 2022; GBD 2019 Mental Disorders Collaborators, 2022; Insel et al., 2010). Current symptom-based diagnostic classifications, while providing a standardized framework for clinical communication and research, do not fully capture the diverse etiologies, clinical trajectories, underlying neurobiological mechanisms, and treatment responses observed among individuals sharing the same diagnosis (Beijers et al., 2019; Cuthbert & Insel, 2013; Insel et al., 2010).

The heterogeneity of mood disorders can be observed from several perspectives. On one hand, patients can exhibit similar clinical features or symptom patterns that may arise from distinct underlying mechanisms, limiting the ability of these phenotypic characteristics to differentiate between etiologically distinct patient subgroups (Beijers et al., 2019; Goldberg, 2011; Hasler, 2010). On the other hand, individuals with an identical

diagnosis of MDD or BD can present with different symptoms, risk factors, comorbidity rates, and treatment outcomes (Lynall & McIntosh, 2023), suggesting that this phenotypic variance can cover underlying biological differences, directly contributing to suboptimal treatment selection, inconsistent research findings, and a lack of reliable biomarkers.

Such complexity strongly suggests the existence of several disorder subtypes related to specific etiologies, which, although converging on the same diagnosis, exhibit a broad spectrum of phenotypic variation across the behavioral, cognitive, and clinical domains. Therefore, effectively understanding and addressing this inherent heterogeneity is crucial for advancing psychiatry toward a precision medicine framework, which aims to develop individualized treatment strategies and identify robust, objective biomarkers that can guide therapeutic decisions for these complex conditions (van Dellen, 2024). The subsequent sections will hence provide a comprehensive overview of the complexity and heterogeneity of mood disorders across various phenotypic, endophenotypic, and genetic levels.

1.2.1 Clinical heterogeneity

The clinical presentation of mood disorders is extremely varied, contributing significantly to their heterogeneity. Within MDD, patients exhibit a wide range of symptom profiles, including varying combinations of core depressive symptoms, as well as specifiers such as anxious distress, melancholic features, atypical features, or psychotic features (American Psychiatric Association, 2022). This leads to a vast number of possible symptom profiles that can qualify for an MDD diagnosis. Indeed, when considering the nine core diagnostic criteria outlined in the DSM-5, 227 distinct combinations of symptoms can meet the threshold for a diagnosis of MDD (Zimmerman et al., 2015). If variations in sleep, appetite, and psychomotor activity are further differentiated by their directional extremes, the number of symptom profiles increases to 945 (Fried & Nesse, 2015). Expanding this analysis to include the various subcomponents of all eight non-mandatory symptom domains yields approximately 16,400 unique symptom combinations that meet the diagnostic criteria for MDD (Fried & Nesse, 2015).

The substantial clinical heterogeneity observed in MDD is further mirrored by the diversity of instruments developed and used to assess depressive symptom severity. For instance, Fried (2017) systematically examined seven commonly used depression rating

scales, including the Hamilton Depression Rating Scale (HAM-D), Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), Patient Health Questionnaire-9 (PHQ-9), Quick Inventory of Depressive Symptomatology (QIDS), Hospital Anxiety and Depression Scale (HADS), and the Montgomery-Åsberg Depression Rating Scale (MADRS). The study revealed that all these instruments collectively encompass 52 distinct depressive symptoms, with limited overlap across scales, and many symptoms are assessed by only one or two instruments (**Figure 1**). This finding emphasizes the fragmented and non-standardized nature of symptom coverage in depression assessment, highlighting how differences in rating scales' content may influence both clinical evaluations and research outcomes. Consequently, the lack of consensus in measurement tools not only reflects the underlying heterogeneity of MDD but may also contribute to inconsistencies in diagnosis, treatment planning, and the identification of reliable biomarkers, thereby posing critical challenges to the replicability and generalizability of depression research (Fried, 2017).

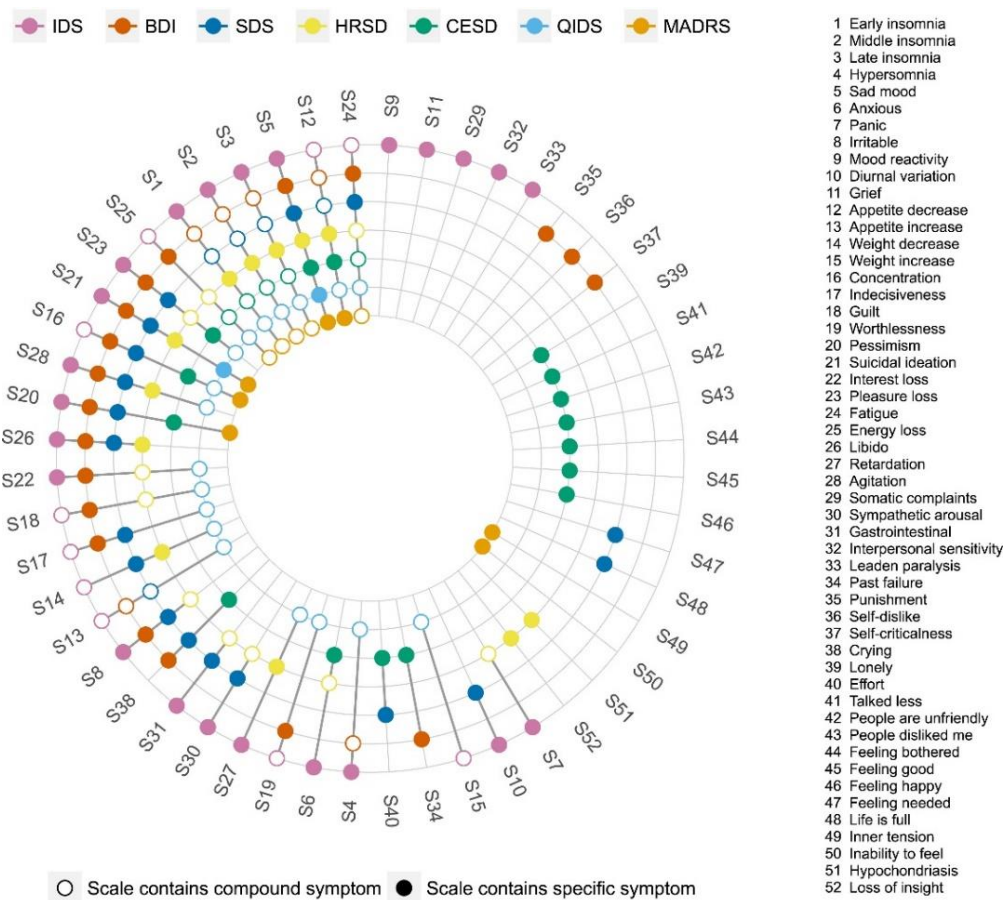


Figure 1. Co-occurrence of 52 depression symptoms across 7 depression rating scales. Reprinted from Fried (2017) with permission from Elsevier (License Number: 6050311490352).

Beyond symptom presentation, significant variability is observed in the comorbidity of mood disorders with other psychiatric and medical conditions. Indeed, it is estimated that approximately 75% of individuals diagnosed with MDD also meet criteria for at least one additional neuropsychiatric condition (Buch & Liston, 2021). The most frequently co-occurring disorders for both MDD and BD include generalized anxiety disorder, post-traumatic stress disorder (PTSD), specific phobias, and substance use disorders, with notable prevalence also observed for obsessive-compulsive disorder (OCD), attention-deficit/hyperactivity disorder (ADHD), and various personality disorders (Arnaud et al., 2022; GBD 2019 Mental Disorders Collaborators, 2022; Kessler et al., 2005; Léda-Rêgo et al., 2024; Nierenberg et al., 2023; Yatham et al., 2018). These elevated rates of comorbidity suggest the potential involvement of shared or transdiagnostic mechanisms that may underlie not only the diverse symptomatology of mood disorders but also the overlapping features observed in related psychiatric conditions (Buch & Liston, 2021). In addition, the high rates of comorbidity with psychiatric disorders affect diagnosis, prognosis, and treatment. For instance, individuals with high somatic anxiety or somatic depression symptoms often report the highest levels of disability and distress, highlighting how specific symptom clusters influence functional impairment (Lin et al., 2025; Morin et al., 2020). Moreover, co-occurring conditions can profoundly impact treatment efficacy and long-term outcomes, necessitating a more tailored diagnostic and therapeutic approach than traditional categorical classifications allow (Cuijpers et al., 2023).

The clinical overlap with physical health conditions is equally significant, particularly with cardiovascular and metabolic diseases, which can lead to poorer adherence to treatment (Gonzalez et al., 2008), difficulties with self-care activities (Lin et al., 2004), increased healthcare costs (Ciechanowski et al., 2000), and a rise in hospital admissions and complications (Nouwen et al., 2019). The relationship between depression and severe medical comorbidities has been widely recognized as bidirectional, with each condition increasing the risk for the other. For instance, a Danish registry cohort meta-analysis revealed that an MDD diagnosis was associated with an increased hazard ratio (HR) of subsequent ischemic heart disease (HR: 1.63, 95% CI: 1.36-1.95) and stroke (HR: 1.94, 95% CI: 1.63-2.30), while pre-existing ischemic heart disease (HR: 1.79, 95% CI: 1.43-2.23) and stroke (HR: 2.62, 95% CI: 2.09-3.29) were linked to a higher risk of

later MDD (Wium-Andersen et al., 2020). Similarly, individuals with MDD have a higher risk ratio (RR) of T2D (RR: 1.18, 95% CI: 1.12-1.24) (Graham et al., 2020), while those with T2D show a higher risk of MDD (RR: 1.15, 95% CI: 1.02-1.30) (Mezuk et al., 2008). Despite large-scale meta-analyses of prospective cohort studies suggesting this reciprocal link between MDD and several physical comorbidities, recent Mendelian randomization studies point to a unidirectional genetic relationship. Indeed, these studies indicate that the genetic predisposition for MDD is associated with an increased risk for coronary artery disease (OR: 1.26, 95% CI: 1.10-1.43) (Tang et al., 2020), small vessel stroke (OR: 1.33, 95% CI: 1.08-1.65) (Cai et al., 2019), myocardial infarction (OR: 1.15, 95% CI: 1.07-1.23) (Li et al., 2022), T2D (OR = 1.22, 95%CI 1.09-1.36) (Tao et al., 2023), and metabolic syndrome (OR: 1.38, 95% CI: 1.17-1.64) (Zhang et al., 2021). However, the genetic liability for these physical conditions did not appear to increase MDD risk, thus suggesting that the underlying mechanisms of these conditions are complex and involve several shared pathophysiological pathways beyond genetics. These include chronic low-grade inflammation, evidenced by elevated levels of pro-inflammatory cytokines and high concentrations of C-reactive protein (CRP), which contribute to both mood dysregulation and atherosclerosis (Köhler et al., 2017; Osimo et al., 2019). Furthermore, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in mood disorders, which has been implicated in their onset, symptom profile, severity, chronicity, and treatment response (Jurueña et al., 2018; Zajkowska et al., 2022), can also lead to chronic hypercortisolemia, which promotes central obesity and insulin resistance, key features of metabolic syndrome (Pasquali & Vicennati, 2000). Finally, unhealthy lifestyle behaviors, such as poor diet, physical inactivity, alcohol consumption, and smoking, are also more prevalent in individuals with MDD and BD (Firth et al., 2018; Fornaro et al., 2022; Schuch et al., 2017; Sullivan et al., 2005) and serve as common risk factors for these medical conditions (Berk et al., 2023).

Cognitive functioning also represents a core dimension of clinical heterogeneity in mood disorders. Specifically, deficits in attention, memory, executive functions, and processing speed are frequently observed in both MDD and BD, but their severity and persistence differ across individuals and diagnostic groups. Broadly speaking, cognition in mood disorders can be differentiated into "hot" (i.e., emotion-related) and "cold" (i.e., non-emotional) domains (Douglas et al., 2020). While emotional biases are particularly

linked to illness onset and maintenance, cold cognitive impairments, such as deficits in executive functioning and working memory, often persist into remission and affect up to 50% of patients (Douglas et al., 2020; Galimberti et al., 2020). These impairments disrupt everyday functioning and remain even when mood symptoms improve (Woo et al., 2016), underscoring their trait-like quality in many patients, as well as the need for targeted interventions that extend beyond mood symptom management. Distinct patterns of cognitive heterogeneity seem to emerge between disorders. For instance, MDD is marked by negative biases in emotional processing, deficits in verbal learning and decision-making, with impairments that are often state-dependent, worsening during acute episodes, and partly resolving in remission (Douglas & Porter, 2009; Godlewska & Harmer, 2021). In contrast, cognitive dysfunctions in BD include deficits in emotion recognition, memory consolidation, and executive control, particularly among patients with psychotic features (Bora et al., 2010; Martínez-Arán et al., 2004). Moreover, they tend to be more enduring and detectable even in euthymic states and appear to accumulate with the illness course (Latalova et al., 2011). However, across both disorders, greater symptom severity has been consistently associated with poorer performance in verbal memory, executive functioning, and processing speed (Cusi et al., 2012). Such variability is clinically significant in real-world settings, as cognitive dysfunction strongly predicts occupational and social disability (Douglas et al., 2020), highlighting the need to recognize these heterogeneous cognitive profiles as essential for identifying patient subtypes and designing interventions that target functional recovery (e.g., neurocognitive rehabilitation) beyond mood stabilization.

Treatment response to standard interventions, including pharmacotherapy and psychotherapy, is also highly variable among individuals affected by mood disorders (Rush et al., 2006; Thase & Connolly, 2019; Trivedi et al., 2006). A considerable proportion of patients experience non-response or only partial remission, leading to a chronic and relapsing course of illness (Buch & Liston, 2021; Ionescu et al., 2015; McIntyre et al., 2023). For instance, only about one-third of MDD patients achieve remission with their first prescribed medication, with many requiring over a year of repeated trials to find an effective treatment (Dodd et al., 2021). Similarly, 26.4% to 28.3% of individuals with BD are found to be treatment-resistant, with several patients continuing to experience high rates of mood recurrences or significant residual symptoms

despite pharmacological treatment (Diaz et al., 2022). This variability in treatment outcomes again underscores the need to identify clinical subtypes that may respond differentially to specific interventions, thereby avoiding the current “trial-and-error” approach to treatment selection, which often prolongs suffering, increases the risk of side effects, and leads to significant societal costs (Pérez-Sola et al., 2021).

Lastly, individuals with mood disorders exhibit a high heterogeneity in the longitudinal course of their illness, including differences in age of onset – ranging from adolescence to young adulthood and late-life – frequency and duration of episodes, and the temporal dynamics between mood episodes and euthymic states (Buch & Liston, 2021; Dohm et al., 2017). These dynamics encompass patterns such as dysthymia, ultradian cycling, variability in episode duration and length of remission, as well as phenomena like “kindling” and cycle acceleration, all of which are hypothesized to have distinct neurobiological underpinnings (Post, 2007; Post et al., 2003; Toenders et al., 2019). For instance, earlier onset of depression has been associated with greater symptom severity and increased recurrence rates, and may reflect different biological pathways compared to later-onset depression (Kozel et al., 2008; Perlis et al., 2009; Sung et al., 2013; Toenders et al., 2019; Zisook et al., 2007).

1.2.2 Neurobiological heterogeneity

From a neurobiological perspective, mood disorders show a high heterogeneity in both brain structural and functional underpinnings, which are considered intermediate phenotypes (i.e., endophenotypes) resulting from the interaction of genetic and environmental factors (Buch & Liston, 2021). Rather than reflecting dysfunctions in isolated brain regions, the etiopathogenesis of mood disorders involves complex alterations in large-scale brain networks that regulate emotion, cognition, and executive control. For instance, large-scale neuroimaging studies have consistently shown that these disorders are characterized by widespread disruptions in cortico-limbic and fronto-parietal circuits, despite considerable heterogeneity in findings across individuals, illness phases, and diagnostic subtypes.

With regard to structural alterations, converging evidence from magnetic resonance imaging (MRI) studies demonstrates cortical thinning in the medial orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), ventromedial prefrontal cortex (vmPFC), and

insular regions in both MDD and BD (Hibar et al., 2018; Schmaal et al., 2017). These regions are strongly connected with the limbic system, both at structural and functional levels, supporting the hypothesis that cortico-limbic dysfunction underlies core affective symptoms of mood disorders (Vai et al., 2019).

Multiple meta-analyses found reduced cortical thickness in frontal regions in MDD. For instance, an early meta-analysis by Koolschijn et al. (2009) involved 64 structural MRI studies and reported significant volumetric reductions in the ACC and the OFC of MDD patients, with grey matter (GM) reduction in the ACC related to the course of the illness, as later found by the meta-analytic study of Lai (2013). This pattern has also been confirmed by the largest existing MRI study comparing 2148 adults with MDD to 7957 healthy controls, conducted by the Enhancing Neuro Imaging Genetics through Meta-Analysis (ENIGMA) consortium (Schmaal et al., 2017). However, the same study did not observe this cortical thinning pattern in adolescents with MDD, which conversely showed reduced surface areas in primary and higher-order sensory and motor areas, medial OFC, and superior frontal gyrus (Schmaal et al., 2017), suggesting that distinct morphological alterations can characterize the MDD population depending on its developmental age.

A widespread reduction in cortical thickness has also been demonstrated in BD by the ENIGMA BD Working Group, who compared 1837 adults affected by BD with 2582 matched healthy controls and identified thinner cortical GM in bilateral frontal, temporal, and parietal regions, with the strongest effect sizes being found in left pars opercularis, fusiform gyrus, and rostral middle frontal cortex (Hibar et al., 2018). These findings were further confirmed by a recent meta-analysis, which included 649 BD patients and 818 controls and observed significant reductions in cortical thickness in the left insula, left inferior and superior frontal gyrus, and bilateral ACC (Zhu et al., 2022). Remarkably, cortical thinning in BD seems to be modulated by age and illness duration, with more pronounced effects observed in older patients and those with prolonged illness trajectories (Berk et al., 2017).

Regarding subcortical regions, hippocampal atrophy is one of the most consistently reported subcortical abnormalities in both MDD and BD. Indeed, a meta-analysis from the ENIGMA consortium showed a nearly 2% volume reduction in the hippocampus of 1728 MDD patients, as compared to 7199 controls, with greater effects in early-onset or recurrent MDD (Schmaal et al., 2016). Additional research suggested this loss to be

associated with symptom persistence and recurrence (MacQueen et al., 2008), even though some studies did not find direct correlations between hippocampal volume and disease severity (Malykhin et al., 2010). Consistent findings of decreased hippocampal volumes have also been found in BD, with no differences among BD-I and BD-II subtypes (Janiri et al., 2019; Schmaal et al., 2016). According to the “neurotrophic and synaptogenic hypothesis of depression”, these findings might be explained by the chronic HPA axis activation and the elevated glucocorticoid levels often observed in mood disorders, which may compromise neurogenesis and structural integrity in the hippocampus across the illness course (Duman & Duman, 2015). In line with this hypothesis, neuroimaging studies support a neuroprotective role of antidepressant and lithium treatment, which conversely may increase hippocampal volume due to their neurotrophic effects (López-Jaramillo et al., 2017).

Findings regarding the amygdala are more controversial. While early research reported smaller amygdala volumes in chronic MDD (Sheline et al., 1998), subsequent studies have identified either increases, reductions, or no volumetric differences with healthy controls, often depending on illness phase and duration (Frodl et al., 2003; Kim et al., 2021; Lorenzetti et al., 2009; Schmaal et al., 2016; Tesen et al., 2021; Zhang et al., 2016). Likewise, contradictory findings have been found in BD. For instance, some studies in adults with BD reported either an increase or no change in amygdala volumes (Altshuler et al., 2000; Chang et al., 2005; Hajek et al., 2009), while a more recent ENIGMA BD large-scale analysis involving 1710 BD patients and 2594 healthy controls found reduced amygdala volumes in BD (Hibar et al., 2016). In contrast, decreased volumes in the amygdala have been consistently observed in adolescents with BD (Pfeifer et al., 2008). Beyond clinical course and age, these incongruences may reflect the anatomical and functional heterogeneity of the amygdala, which can be divided into multiple nuclei (Sah et al., 2003). Indeed, recent high-resolution segmentation techniques suggest that amygdala nuclei show differential connectivity patterns, as compared to healthy controls (Brown et al., 2020), and volumetric sensitivity to depression severity (Brown et al., 2019b).

Another widely investigated structural correlate of mood disorders is white matter integrity. Several diffusion tensor imaging (DTI) studies have examined microstructural white matter abnormalities in both disorders, revealing a particular involvement of the

corpus callosum, cingulum bundle, and uncinate fasciculus in their etiopathogenesis. Common measures derived from DTI include fractional anisotropy (FA), which reflects uniformity and compactness of fiber bundles, axial diffusivity (AD), which represents axonal number and organization, mean diffusivity (MD), a measure of membrane density, and radial diffusivity (RD), a measure of myelination (Alexander et al., 2011). A meta-analytic study by the ENIGMA MDD Working Group, comparing 1305 MDD patients and 1602 healthy controls, demonstrated significantly reduced FA across numerous tracts, including the anterior corona radiata, corpus callosum, cingulum, fornix, and inferior fronto-occipital fasciculus (van Velzen et al., 2020). Reductions in FA were accompanied by increased RD in the same tracts, suggesting microstructural alterations in myelination or glial morphology (Song et al., 2005). Another large-scale study confirmed these patterns, reporting reduced FA in thalamic radiations and interhemispheric tracts, thereby supporting the etiopathogenetic hypothesis of reduced integrity in key tracts of brain networks (e.g., including PFC and thalamus) that are involved in emotion regulation, reward processing, and executive control (Shen et al., 2017).

Analogous white matter dysconnectivity patterns have also been found in BD. FA reductions have been observed in the corpus callosum and fronto-limbic association fibers such as the superior fronto-occipital fasciculus and the longitudinal fasciculi (Barysheva et al., 2013). These alterations have been linked to cognitive deficits in working memory, executive function, and psychomotor performance (Poletti et al., 2015). The largest DTI study in this regard was conducted by the ENIGMA BD working group, which analyzed 1,482 BD patients and 1,551 healthy controls. The analyses confirmed widespread reductions in FA among BD patients, which were negatively associated with illness duration, with the stronger effect sizes being observed within the corpus callosum and cingulum (Favre et al., 2019). Similar interhemispheric disconnections have also been observed in schizophrenia (SCZ) (Kelly et al., 2018) and MDD (Wise et al., 2016), thereby pointing to possible shared transdiagnostic substrates, as also confirmed by subsequent transdiagnostic research (Tao et al., 2022).

On the functional side, neuroimaging studies including both task-based and resting-state functional MRI (fMRI) support the presence of cortico-limbic dysregulation in mood disorders. Resting-state functional connectivity (rsFC) studies in both MDD and BD consistently point towards large-scale network dysfunctions, implicating key

functional networks such as the default mode network (DMN), salience network (SN), and frontoparietal network (FPN). A meta-analysis by Kaiser et al. (2015b) investigating rsFC in MDD revealed hypoconnectivity within the FPN, a system crucial for cognitive control and emotion regulation, as the major finding across 27 studies. This reduced connectivity was often observed between FPN and regions of the dorsal attention network (DAN), which are involved in external attention and cognitive control (Choi et al., 2012; Yeo et al., 2011). Conversely, hyperconnectivity was frequently reported within the DMN, associated with internally-oriented and self-referential thought, and between DMN and the FPN, suggesting a bias towards internal rumination (Kaiser et al., 2015a). Despite these consistent findings, more recent large-scale meta-analyses found these functional effects to be modest and variable. For instance, a recent mega-analysis failed to replicate the results of Kaiser et al. (2015b) and, conversely, highlighted a decreased connectivity between sensory networks and the SN (Javaheripour et al., 2021). Moreover, a recent pooled analysis from Tozzi et al. (2021) found only a small reduction of DMN connectivity in MDD (effect size $g \approx 0.25$). Notably, this reduction was significant only at the meta-analytic level, since individual cohorts showed wide variability and overlapping confidence intervals, indicating that DMN hypoconnectivity may not be a robust marker in every patient (Tozzi et al., 2021).

Resting-state fMRI (rs-fMRI) research in BD also reports widespread functional network imbalances, despite yielding inconsistent findings. For instance, some research observed patterns of either increased or decreased activation within and between large-scale networks, including DMN, FPN, and SN (Cattarinussi et al., 2022a; Gong et al., 2021). On the other hand, other studies have found no significant differences between individuals with BD and healthy controls, suggesting that this discrepancy could be attributed to the heterogeneity in patients' mood states (i.e., depressed vs. manic/hypomanic states) and their clinical characteristics (Syan et al., 2018). Both consistent and divergent findings also emerged from recent meta-analyses focused on alterations in neural activity within specific regions of interest (ROIs), including amplitude of low-frequency fluctuations (ALFF), fractional ALFF (fALFF), and regional homogeneity (ReHo) during resting-state in BD patients. For instance, Schumer et al. (2023) identified a convergence of findings across 150 resting-state experiments of altered functional connectivity in the right ventral posterior cingulate cortex (PCC) in BD

patients, a core node of the DMN, which was particularly evident during depressed mood states. Chen et al. (2022a) reported more widespread alterations, observing increased resting-state activity in regions such as the left middle frontal gyrus, right inferior frontal gyrus, insula, and right superior frontal gyrus, and bilateral striatum, alongside with decreased activity in the left middle temporal gyrus, superior temporal gyrus (STG), post-central gyrus, and cerebellum, and bilateral precuneus. Finally, a coordinates-based meta-analysis performed by Nan et al. (2024) also noted increased resting-state activity in the amygdala, putamen, striatum, and insula of BD patients, yet these findings did not survive multiple statistical corrections.

The heterogeneity of findings is even more pronounced when looking at the functional correlates of mood disorders during task-based fMRI (t-fMRI), possibly due to the high variance in experimental protocols and task designs. Indeed, despite numerous functional studies reporting altered activations in frontal, limbic, and temporal regions during both emotional and cognitive tasks, a meta-analysis of 99 t-fMRI experiments in MDD was not able to identify any significant pooled difference between patients and healthy subjects (Müller et al., 2017). However, a recent meta-analysis, including 120 studies and comprising over 3,000 patients, suggested increased activity in the bilateral STG and left insula, as well as decreased activity in regions such as the left dorsolateral prefrontal cortex (dlPFC), caudate, and right putamen (Wang et al., 2023). During cognitive tasks, particularly those assessing executive function or working memory, MDD patients often show frontal hypoactivation compared to healthy controls, hence reflecting an impaired top-down regulation (Pilmeyer et al., 2022). However, the same study also reported hyperactivation in the same brain areas, particularly in well-performing patients, which may reflect compensatory recruitment of additional cognitive resources. Pilmeyer et al. (2022) also meta-analyzed findings across emotion-processing tasks, observing limbic hyperactivity, particularly in the amygdala and ACC. Interestingly, Wang et al. (2023) compared findings between current and remitted MDD (rMDD) and found shared hyperactivation in the right temporal pole and STG, suggesting persistent neural alterations beyond symptom remission. In contrast, rMDD patients demonstrated increased activation in the right striatum and caudate, and reduced activity in the left superior frontal gyrus, possibly reflecting recovery-associated plasticity (Wang et al., 2023).

In BD, task-based fMRI meta-analyses highlight condition-dependent alterations. For instance, during emotional processing tasks, individuals with BD consistently exhibit hyperactivation in the left amygdala, especially when responding to emotionally salient stimuli of mixed valence (Schumer et al., 2023). In addition to the amygdala, the same hyperactivation has also been repeatedly found in the caudate, precentral gyrus, middle frontal gyri, and subgyrus (Ahmed et al., 2023). These findings align with clinical observations of affective lability and heightened emotional reactivity in BD, suggesting that abnormal limbic engagement may underlie difficulties in regulating mood states (Ahmed et al., 2023; Schumer et al., 2023). Of note, this limbic hyperactivation has been observed to be prolonged over time, as an altered amygdala habituation to emotional stimuli has been found among BD patients, thus confirming the role of an imbalanced cortico-limbic function in sustaining emotional dysregulation in BD (Vai et al., 2023). In the cognitive domain, especially during working memory and executive functioning tasks, BD patients show altered recruitment of prefrontal and parietal regions. For instance, hypoactivation of the left superior and right inferior parietal lobules has been observed across 222 emotional task-based studies, alongside hyperactivation in the left medial OFC, potentially reflecting inefficient or compensatory cognitive control mechanisms (Schumer et al., 2023). Additionally, a meta-analysis conducted by Mesbah et al. (2023) also reported increased activation in the subgenual ACC and vmPFC during working memory tasks in BD. According to the authors, these regions are involved in integrating emotional salience with executive control, and their dysregulated engagement may contribute to the cognitive-affective disturbances characteristic of the disorder. Reward processing deficits also emerge as a core feature in BD, with meta-analytic evidence of 9 t-fMRI studies revealing increased activation in the left OFC during reward anticipation (Mesbah et al., 2023). Indeed, the OFC plays a central role in encoding reward value and expectation, and its hyperactivity may reflect a neural substrate for the heightened reward sensitivity and impulsive behavior often seen in manic or hypomanic states (Alloy et al., 2016). Taken together, these findings underscore that neural dysfunctions in BD are not uniform across tasks but are strongly modulated by the cognitive or emotional context.

In conclusion, despite a few research studies directly investigating the neurobiological heterogeneity within mood disorders, neuroimaging studies comparing

healthy controls versus patients reveal robust yet heterogeneous structural and functional abnormalities in mood disorders. While alterations in prefrontal, limbic, and white matter circuits are consistently implicated, their expression seems to vary across clinical subtypes, illness stages, and experimental paradigms. These findings hence emphasize the necessity for stratified neuroimaging approaches that account for this heterogeneity and support efforts toward biologically informed subtyping.

1.2.3 Genetics and polygenic contributions

The genetic architecture of mood disorders is inherently complex and highly polygenic. Twin and family studies consistently underline the significant heritability of these disorders, with genetic factors accounting for approximately 37% of the risk for MDD (Kendler et al., 2018) and 60-85% for BD (Smoller & Finn, 2003), indicating a greater etiological effect of genes than environment in the latter (Oraki Kohshour et al., 2024). Nevertheless, these conditions are influenced by numerous common genetic variants, each contributing with a small effect, rather than being driven by single genes with large effects (Wray et al., 2018). In this regard, Genome-Wide Association Studies (GWASs) have revolutionized the field by identifying hundreds of genetic loci associated with both MDD and BD. This approach further highlighted the polygenic nature of these disorders and revealed a significant genetic overlap among various psychiatric disorders (Sullivan, 2010). For instance, one of the latest MDD GWASs identified 102 independent genome-wide significant variants at 101 genomic loci, showing correlations with various other diseases and phenotypes, including BD, SCZ, anorexia nervosa, neuroticism, and metabolic traits (Howard et al., 2019). The latest and largest GWAS for MDD, performed by the Psychiatric Genomics Consortium (PGC), included 688,808 individuals with MDD and 4,364,225 controls, and identified 697 significant associations at 635 genomic loci, 293 of which were completely novel. The same study, by conducting a neural cell-type enrichment analysis through published gene-expression datasets, uncovered that the significantly associated variants were implicated in the expression of excitatory, inhibitory, and medium spiny neurons, along with a specifically enriched pathway for the amygdala excitatory neurons (Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium, 2025). However, a significant challenge in MDD GWASs is the variability in case definitions, often relying on broad diagnostic criteria

(e.g., ICD-11) or self-report measures, as well as the intrinsic heterogeneity of the disorder, which significantly restricts the strength and consistency of genetic associations, leading to incongruent findings across studies (Levinson et al., 2014). For instance, a recent GWAS from Nguyen et al. (2022) on UK Biobank subgrouped analysis on MDD patients by clinical features and reported subtype-specific heritability rates for single-nucleotide polymorphisms (SNPs), with genetic correlations ranging from 0.5 to 0.86 among subtypes (**Figure 2**). The results hence indicate the existence of a unique genetic vulnerability characterizing each depressive subtype that cannot be detected when considering depression as a single entity (Nguyen et al., 2022).

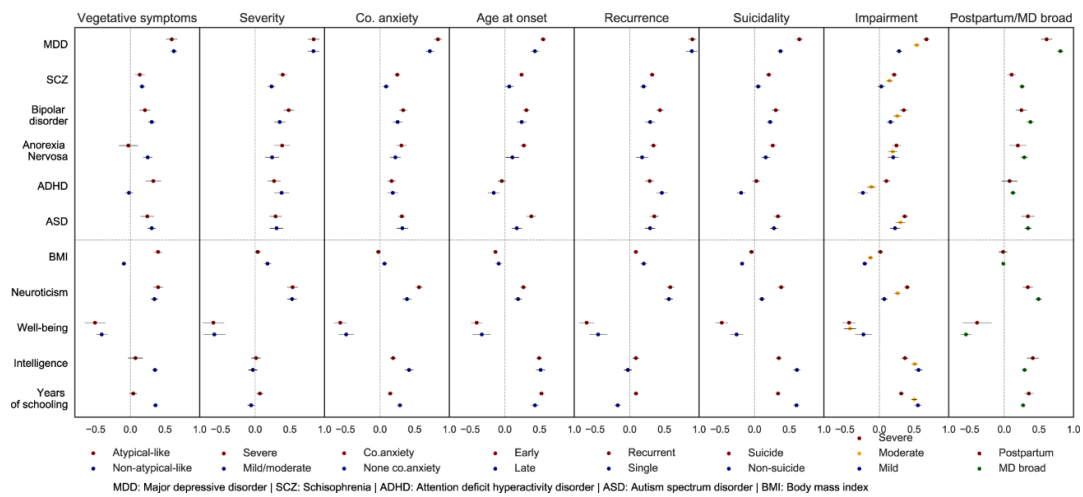


Figure 2. Genetic correlations between MDD subtypes, other psychiatric disorders, and related conditions. Reprinted from Nguyen et al. (2022) with permission from Springer Nature (License Number: 6053930034712).

The largest GWAS conducted by the PGC on BD, involving 58,036 cases with BD and over 2.8 million controls, identified 298 genome-wide significant loci associated with the disorder (O'Connell et al., 2025). The study also performed a single-cell enrichment analyses of brain cell types, suggesting an involvement of the associated variants in the expression of neuronal populations from different brain regions, such as PFC and hippocampal interneurons, as well as pyramidal neurons from the hippocampus (O'Connell et al., 2025), thereby confirming findings reported by the previous PGC-BD GWAS (Mullins et al., 2021). The study also provided evidence of significant shared genetic variation (i.e., pleiotropy) between BD and several psychiatric disorders, with a genetic correlation ranging from 0.14 to 0.85 (**Figure 3**), suggesting a partially common

genetic vulnerability, especially with MDD, PTSD, and SCZ (O'Connell et al., 2025). Moreover, in line with previous GWASs, differences in genetic architecture between BD-I and BD-II were found, with significantly higher SNP heritability in BD-I (O'Connell et al., 2025). Finally, similarly to MDD, partially overlapping but also unique associations have been found depending on BD subtypes, with BD-I demonstrating a stronger genetic correlation with schizophrenia, and BD-II showing a higher correlation with MDD (O'Connell et al., 2025).

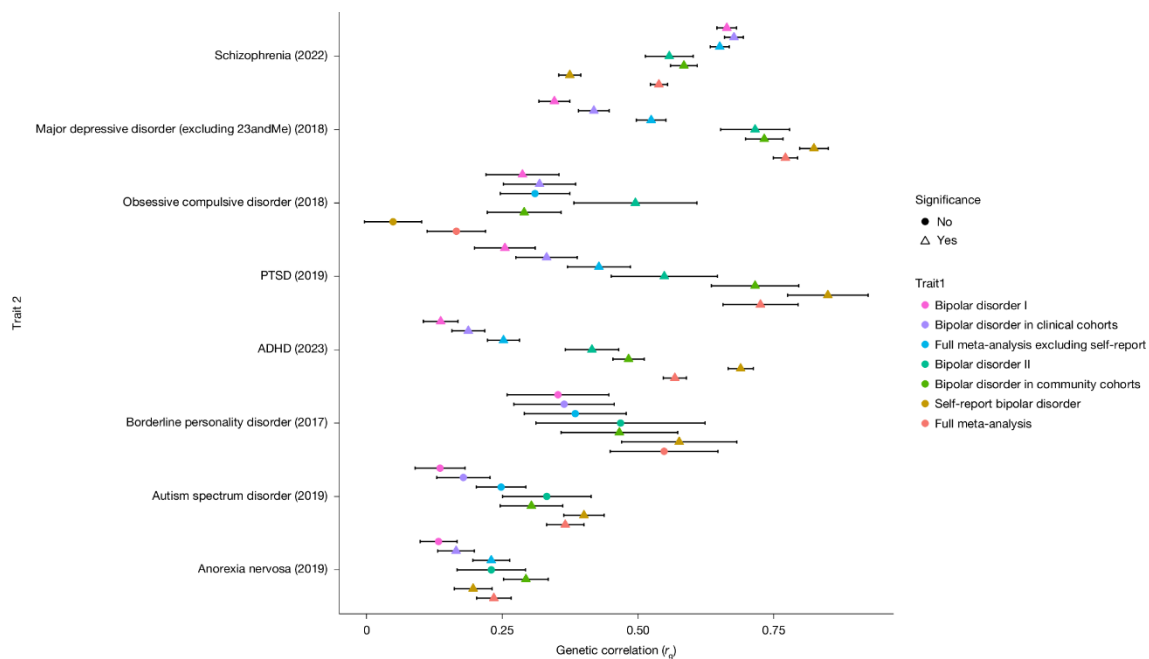


Figure 3. Genetic correlations between BD subtypes and other psychiatric disorders. Reprinted from O'Connell et al. (2025) with permission from Springer Nature (License Number: 6053930443297).

Beyond common genetic variants, the effect of rare or low-frequency genetic variants (i.e., variants present in <1% of the general population or with a minor allele frequency <0.5%) has also been explored in mood disorders, thanks to the progress of whole-exome (WES) and whole-genome sequencing (WGS) technologies (Kendall et al., 2021). However, despite these variants being expected to contribute to the genetics of mood disorders, their association with these conditions appears to be low to moderate (Lee et al., 2014; Yu et al., 2018). Indeed, numerous linkage studies conducted in families with MDD did not detect any causal variants associated with the disorder (Kendall et al., 2021). Moreover, a large WGS study involving 5303 MDD patients and 5337 controls failed to uncover a significant association of individual rare or low-frequency variants

with MDD (CONVERGE Consortium, 2015). Conversely, a significant enrichment of rare variants has been detected in BD, despite most of them being identified in genes derived from GWAS studies on SCZ (Green et al., 2016; Palmer et al., 2022), possibly suggesting that the genetic overlap between BD and SCZ transcends common, low-risk alleles and extends to rare alleles of greater effect (Gordovez & McMahon, 2020).

As previously mentioned, neither rare variants nor the modest effect sizes of common variants detected from GWASs can fully explain the heritability or heterogeneity observed in mood disorders. This has led to the development of polygenic scores (PGSs), which aggregate the effects of thousands or millions of genetic variants across the genome to estimate an individual's genetic predisposition to a disorder or trait (Andreassen et al., 2023; Murray et al., 2021). PGSs represent a cumulative measure of an individual's genetic susceptibility, calculated by summing the effects of numerous risk-associated genetic variants identified through GWASs. These scores have been increasingly leveraged to explore genetic heterogeneity within mood disorders, predict individual risk, and potentially identify biologically distinct patient subgroups that may share common pathophysiological mechanisms (Murray et al., 2021).

For instance, in the context of MDD, PGSs for adult depression have demonstrated utility in predicting the age of onset during childhood and adolescence, thus showing the predictive capability of MDD-PGS for early-onset manifestations of the disorder (Halldorsdottir et al., 2019; Harder et al., 2022). MDD-PGS has also been found to be associated with antidepressant efficacy across various studies, with elevated scores predicting less favorable outcomes in MDD patients treated with SSRIs (Magarbeh et al., 2025; Shao et al., 2025; Ward et al., 2018). Expanding these findings, a systematic review by Meerman et al. (2022) also reported several PGSs for ADHD, personality traits, coronary artery disease (CAD), obesity, and stroke to be significantly associated with antidepressant treatment response in MDD patients. MDD-PGS also exhibited broad associations with numerous psychiatric and medical comorbidities, including cardiometabolic diseases and obesity, suggesting a complex interplay of genetic liabilities (Fang et al., 2022). Other studies employing PGSs have also revealed connections between a genetic predisposition for MDD and specific cognitive profiles. For instance, Thalamuthu et al. (2022) found a significant association between MDD-PGS and the cognitive domains of processing speed, immediate memory, and global cognition, while

also revealing a significant interaction with MDD status, suggesting potential links between the biological heterogeneity of MDD and broader risk for neurodevelopmental disorders. In line with this hypothesis, a cross-disorder PGS analysis also highlighted that genetic liability for ADHD positively predicted the risk of MDD (Du Rietz et al., 2018). Neuroimaging research further connected MDD-PGS to disruptions in GM cortical and white matter networks (Gong et al., 2025), as well as to altered neural responses to reward and punishment in frontal, parietal, and occipital brain regions (Chen et al., 2025). In line with this, a comprehensive systematic review also indicated that MDD-PGSs, as well as those for BD and SCZ, are significantly linked to cortical alterations in prefrontal brain regions not only in clinical populations but also within healthy controls (Cattarinussi et al., 2022b).

Concerning BD, despite some studies finding no direct association between BD-PGS and age at onset (Aminoff et al., 2015), PGSs for BD have been associated with an increased risk of new-onset BD in at-risk offspring, particularly when interacting with parental age of mood disorder onset (Hafeman et al., 2025). BD-PGS has also shown promise in predicting response to ECT (Sigström et al., 2022), yet not consistently for antidepressant response in MDD populations (Tansey et al., 2014). Moreover, BD-PGS has demonstrated strong associations with psychiatric comorbidities like anxiety, substance use disorders, and suicidal ideation. For example, Reginsson et al. (2018) observed a significant interaction between BD-PGS and the odds ratios for alcohol and substance abuse. Similarly, Calafato et al. (2018) identified an association between BD-PGS and psychosis across two independent cohorts, demonstrating that patients with psychotic disorders exhibited significantly higher PGSs for BD. Similarly to MDD, BD-PGS also revealed significant associations with regional grey and white matter volumes, as well as divergent thinking in frontal regions (Jiang et al., 2023b; Takeuchi et al., 2021). Furthermore, other psychiatric PGSs, such as SCZ-PGS and ADHD-PGS, showed shared genetic vulnerabilities with BD, impacting addiction risk, early-onset presentations, and poorer outcomes among BD patients (Grigoriou-Serbanescu et al., 2020; Jiang et al., 2025; Reginsson et al., 2018).

Overall, although PGSs have significantly advanced our understanding of the polygenic architecture of MDD and BD, offering insights into mood disorders' etiology and heterogeneity, clinical presentation, and treatment outcomes, their clinical utility

largely remains restricted to research. Indeed, despite the strong genetic component suggested by the heritability estimates, PGSs alone only explain a modest 1-2% of variance in psychiatric disorders (Lewis & Vassos, 2020), suggesting that the clinical heterogeneity of these conditions, including comorbidities and treatment response rates, may be further accounted for by polygenic factors associated with other traits. These can include PGSs for several psychiatric disorders, medical conditions (e.g., cardiovascular and metabolic dysfunctions), and inflammatory markers, as shared genetic and pathophysiological pathways are implicated in the co-occurrence between psychiatric disorders and physical illnesses (Teixeira et al., 2022). Moreover, the limited variance explained by PGSs alone can suggest a substantial contribution from environmental influences to their etiology and highlight the need for wider and more complex exploration of gene-environment interactions (GxE). In this regard, epigenetic mechanisms, including DNA methylation, histone modifications, and non-coding RNAs, are increasingly recognized as pivotal mediators of GxE, as they provide a molecular link between genetic vulnerability and environmental exposures, particularly early life stress (Nestler, 2014; Penner-Goeke & Binder, 2019; Talarowska, 2020). Indeed, these epigenetic modifications can lead to stable changes in gene expression, influencing critical processes such as brain development, stress response systems (e.g., HPA axis), and neuroplasticity, which, in turn, can increase an individual's susceptibility to depression later in life (Kaufman et al., 2000; Miguel et al., 2019; Park et al., 2019).

In conclusion, the etiology of mood disorders is characterized by a complex interplay of polygenic common variants, rare structural variations, and dynamic GxE interactions modulated by epigenetic mechanisms, hence highlighting the need for a comprehensive integration of genomic and environmental data to advance towards a more stratified and personalized paradigm for prevention and treatment strategies.

1.2.4 Environmental factors

Environmental factors play a pivotal role in the etiology and clinical manifestation of mood disorders, interacting with genetic susceptibility to influence an individual's risk and resilience, as well as contributing significantly to the observed phenotypic and endophenotypic variance of these disorders (Amstadter et al., 2016; Moffitt et al., 2005). Among these factors, stress, in its various forms, is widely recognized as a highly

impactful environmental determinant that can contribute to the onset and maintenance of numerous psychiatric conditions, including depression, anxiety, PTSD, and substance abuse (Dánielsdóttir et al., 2024). Specifically, early life stress (ELS), encompassing experiences such as childhood trauma and dysfunctional familial environment, stands out as a critical risk factor for long-term mental health outcomes (Heim et al., 2010; Nemeroff, 2016; Teicher & Samson, 2013).

An extensive body of literature on ELS highlights the critical role of adverse childhood experiences (ACEs) in impacting individuals' lives. Among ACEs, most studies focused on childhood maltreatment, in particular, which can be classified into five primary categories (Bernstein et al., 2003): physical abuse, which refers to acts of physical aggression by an older individual that pose a risk of harm or result in actual injury to the child; emotional abuse, which involves verbal hostility that threatens a child's emotional well-being, moral development, or sense of self-worth (e.g., humiliation, intimidation, or persistent threats); sexual abuse, encompassing any form of sexual interaction or inappropriate behavior imposed on a child by someone older; emotional neglect, which is the consistent lack of caregivers to meet a child's emotional and psychological needs (e.g., affection, motivation, and support); physical neglect, involving the inability or unwillingness of caregivers to provide essential physical necessities, including adequate nutrition, shelter, medical care, protection, and supervision. Consistent findings indicate that exposure to ACEs represents a significant risk factor for numerous psychiatric disorders, increasing the probability of developing at least one psychiatric disorder in adulthood (Dánielsdóttir et al., 2024). For instance, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) conducted by Sugaya et al. (2012) found that the exposure to childhood physical abuse increased the risk of having anxiety disorders (OR = 1.99, 95%CI: 1.78, 2.22), mood disorders (OR = 1.96, 95%CI: 1.76, 2.19), psychotic disorders (OR = 1.69, 95%CI: 1.35, 2.13), and substance use disorders (OR = 1.61, 95%CI: 1.44, 1.80) later in life.

In the context of mood disorders, exposure to ACEs has been consistently linked to more severe, chronic, and treatment-resistant forms of depression, an earlier age of onset, and increased comorbidity (Aas et al., 2016; Nanni et al., 2012; Wrobel et al., 2022). Specifically, MDD patients with an early history of trauma are characterized by worse clinical course, including a higher number of recurrences, lower treatment response,

increased suicidal risk, earlier age of onset, higher number of depressive episodes, and higher rates of comorbidity with PTSD, substance abuse, and medical conditions (Nanni et al., 2012; Souama et al., 2023; Wrobel et al., 2022). Analogous findings have also been observed in BD, with a history of childhood trauma being associated with earlier age of onset, a heightened risk of attempting suicide, rapid cycling, a higher recurrence of mood episodes, an increased risk of psychosis, and lifetime prevalence of substance abuse (Aas et al., 2016; Etain et al., 2013; Park et al., 2020).

A putative explanation for the impact of ACEs on the clinical outcomes and prognosis of mood disorders relies on their profound and lasting effects on the developing brain and other physiological systems, which thereby increase the susceptibility to psychopathology (Lupien et al., 2009; Teicher & Samson, 2013; Teicher et al., 2016). Indeed, during critical developmental time windows, such as childhood, neural circuits and neurotransmitter systems are particularly responsive to environmental stressors, which interfere with key mechanisms of brain development, including neurogenesis, dendritic and axonal branching, myelination, and synaptic pruning (Hart & Rubia, 2012).

Due to these neurodevelopmental disruptions, Teicher & Samson (2013) have hypothesized the existence of specific trauma-related phenotypes (i.e., “ecophenotypes”), modeled by environmental adversities and characterized by unique neurobiological and clinical profiles. Several neuroimaging findings support this framework, demonstrating that specific categories of early trauma can differentially affect brain structure and function. For instance, individuals exposed to parental verbal aggression have been found to exhibit reduced GM volume in auditory processing areas and altered white matter integrity within the arcuate fasciculus; on the other hand, childhood sexual abuse was associated with decreased GM volume in primary and associative visual brain regions and cortical thinning of somatosensory cortices (Teicher et al., 2016). At the functional level, meta-analytic evidence on fMRI studies found significant hyperactivation of the left superior frontal gyrus and middle temporal gyrus, as well as reduced activation of the left superior parietal lobule and hippocampus in adults with a history of childhood maltreatment (Heany et al., 2018). Nevertheless, a recent systematic review by Cooke et al. (2023), which included more than 200 studies investigating the neurobiological correlates of childhood maltreatment, highlighted that not all individuals experiencing early adversities exhibit brain alterations to the same extent. According to the authors,

this heterogeneity could reflect the existence of biological resilience, defined as a dynamic and multi-system biological process that contributes to enhanced health and behavioral outcomes if subjected to environmental stressors (Cooke et al., 2023; Moreno-López et al., 2020).

Beyond ACEs, stressful life events (SLEs) in adulthood, such as the death of a loved one, job loss, financial adversity, serious illness, and interpersonal conflict, are critical environmental factors that can influence the etiology, course, and prognosis of mood disorders. These experiences, irrespective of whether they are traditionally categorized as negative (e.g., bereavement, divorce) or positive but disruptive (e.g., marriage, childbirth), require significant psychological adjustment and have consistently been linked to depressive symptomatology (Gronewold et al., 2022).

Early studies have demonstrated that recent SLEs significantly increase the likelihood of developing MDD (Kendler et al., 1999; Stegenga et al., 2012), with evidence suggesting that approximately 50% of first-onset episodes are preceded by a severe life event, similar to 22–39% of recurrent episodes (Monroe et al., 2007). Importantly, these stressors also influence the trajectory and the prognosis of the disorder, contributing to the risk of relapse and complicating remission. For instance, Monroe et al. (2019) emphasized that while severe stressors are more commonly linked to first-onset depression, they continue to pose a risk for recurrence, even though their relative influence diminishes over time. Moreover, a recent meta-analysis by Buckman et al. (2022) found that depressed individuals reporting three or more SLEs in the six months before initiating treatment demonstrated significantly poorer treatment outcomes, independent of whether they were experiencing a first or recurrent episode.

The relationship between SLEs and the illness course of BD has also been well-established. A pioneering review by Johnson & Roberts (1995) reported that individuals with BD encounter a significantly greater number of SLEs before acute mood episodes than during euthymic phases or in comparison to healthy controls. These findings were confirmed by a subsequent meta-analysis of Lex et al. (2017), highlighting that patients with BD exhibit more life stress preceding episodes than both physically ill and healthy individuals. Moreover, stressful experiences independent of the illness (i.e., not caused by the individual's symptoms) were shown to accelerate relapse and delay recovery (Johnson, 2005). Recent longitudinal studies further support the association between

SLEs and adverse clinical features in BD. For instance, in a large-scale cohort study, Av Kák Kollsker et al. (2022) observed that patients with newly diagnosed BD had significantly more recent and lifetime SLEs than both unaffected relatives and healthy controls. Moreover, those with greater exposure to severe life stress had more prior hospital admissions, longer delays in diagnosis, heightened anxiety, increased self-reported depressive symptoms, and impairments across occupational, financial, and interpersonal domains, as well as more frequent suicide attempts (Av Kák Kollsker et al., 2022), aligning with prior evidence linking both early and adult stressors to suicidal behavior in BD (Carballo et al., 2008; Pompili et al., 2011).

At the biological level, chronic exposure to stress induces a cascade of alterations in various body systems, particularly the HPA axis. The HPA axis is the central neuroendocrine system orchestrating the organism's response to stress, with its activation resulting in the release of glucocorticoids (primarily cortisol in humans) into systemic circulation (Herman et al., 2016). Under normal physiological conditions, HPA axis activity is regulated through a negative feedback loop, ensuring the return to homeostasis once the stressor is resolved. However, chronic or repeated exposure to stress can disrupt this feedback mechanism, leading to prolonged HPA axis activation and persistent glucocorticoid hypersecretion (Jurueña et al., 2020; Lee & Sawa, 2014).

This dysregulation significantly affects the integrity of the nervous system. Indeed, an excessive release of glucocorticoids impairs neuroplastic processes by disrupting brain-derived neurotrophic factor (BDNF) signaling and altering glutamatergic transmission, thereby contributing to synaptic loss and dendritic retraction, particularly in the hippocampus and PFC (Popoli et al., 2011). These structural changes align with post-mortem findings in individuals with mood disorders, including reductions in synapse density and dendritic complexity in several limbic and cortical structures (Duman & Duman, 2015).

Notably, the effects of chronic stress on the HPA axis extend beyond immediate neurochemical imbalances. Persistent activation alters gene expression and neural architecture through epigenetic modifications, thereby embedding stress-related vulnerabilities into biological systems (Bertollo et al., 2025). Although the majority of this evidence is derived from early life adversity, similar pathophysiological mechanisms are activated by sustained adult stress, reinforcing the role of the HPA axis as a critical

mediator between environmental exposure and the development of mood disorders (Lee & Sawa, 2014).

In conclusion, environmental factors, including ACEs and SLEs, exert a profound influence on the etiology and phenotypic expression of mood disorders, often interacting with genetic predispositions. These exposures induce lasting neurobiological changes, including alterations in brain structure and function and HPA axis dysregulation, contributing to increased vulnerability and a more severe, chronic disease course. Understanding the specific types and timing of these environmental influences, their neurobiological consequences, and their interplay with genetic factors can be essential for identifying distinct patient subgroups, tailoring clinical evaluations, and developing trauma-informed and personalized interventions in mood disorders.

1.2.5 Implications for research and clinical practice

The extensive heterogeneity of mood disorders, manifesting in wide interindividual variability across symptom profiles, clinical trajectories, neurobiological mechanisms, genetic predispositions, and environmental risk factors, as investigated in the previous paragraphs, has profound implications for both the research framework and clinical practice. For instance, the complexity of these conditions renders these psychiatric disorders difficult to define, diagnose, and treat using conventional categorical frameworks such as DSM-5-TR or ICD-11 (Newson et al., 2020; Williams et al., 2024).

These traditional diagnostic systems, which rely primarily on the presence and enumeration of symptoms, allow for significant within-diagnosis variability and are suboptimal in predicting illness courses, thereby hindering clinical decision-making and contributing to low reliability in mood disorder prognosis (Newson et al., 2020). As a result, patients often receive multiple or shifting diagnoses over time, facing “trial and error” approaches to treatment selections, with ineffective treatments in turn leading to higher treatment resistance rates and prolonged illness course (Pérez-Sola et al., 2021). In parallel, the same disorder may present with markedly different clinical profiles across individuals, complicating accurate diagnosis and hampering the outlining of effective treatment plans (Lynall & McIntosh, 2023). Furthermore, inconsistencies in the tools used for mental health assessment, ranging from clinical interviews to standardized questionnaires, exacerbate diagnostic variability and challenge the reproducibility of

findings across clinical settings (Fried, 2017; Newson et al., 2020). Indeed, such variability further hampers traditional clinical trials and research studies attempting to identify candidate biomarkers, which often fail to account for intragroup heterogeneity, leading to weak effects and findings that are hardly replicable (Belleau, 2022; Wallstrom et al., 2013)

In the domain of therapeutics, the recognition of heterogeneity suggests the need to abandon the “one-size-fits-all” paradigm in favor of biologically informed, stratified treatment development (Tozzi et al., 2024). Historically, relying on symptom-based nosology led to high treatment resistance rates and modest response to standard antidepressants (Kessler et al., 2017). Instead, the integration of biological markers into clinical trials can enhance predictive power, reduce variability, and enable the development of drugs tailored to specific pathophysiological circuits (Scangos et al., 2023). For example, inflammation-targeting agents may be more effective in patients with immune-related depression, whereas modulators of synaptic plasticity may benefit other neurobiological subtypes (Alshehri et al., 2023; Tang et al., 2025).

To promote this progress, a methodological and experimental shift is needed. For instance, research frameworks such as the Research Domain Criteria (RDoC) and the Hierarchical Taxonomy of Psychopathology (HiTOP) have been advanced as alternatives to conventional diagnostic systems in psychiatry. On the one hand, the RDoC initiative suggests a dimensional approach to psychopathology, proposing transdiagnostic core functional domains – ranging from genetic and molecular processes to observable behaviors – rather than rigid diagnostic categories (Insel et al., 2010). On the other hand, the HiTOP model posits a general liability factor (i.e., “*p-factor*”) underlying psychopathology, within which more specific symptom clusters are organized into a multilevel hierarchy (Kotov et al., 2017). Both approaches share the aim of leveraging recent neuroscientific and clinical research findings to elucidate the biological mechanisms of psychiatric conditions, thereby guiding the evolution of diagnostic classifications and the discovery of novel treatment targets (Michellini et al., 2021).

Beyond these theoretical approaches, innovations in the technological field also support the advancement towards a precision psychiatry framework. For instance, machine learning (ML) techniques enable the identification of latent structures in high-dimensional datasets, while allowing for predictions at the single-subject level, thereby

revealing patterns and relationships that overcome traditional statistics (Bzdok & Meyer-Lindenberg, 2018; Chen et al., 2022b). Normative modeling, in addition, evaluates individual deviations from reference populations, offering insights beyond binary case-control comparisons (Marquand et al., 2019). Moreover, omics technologies, including genomics, transcriptomics, epigenomics, and metabolomics, facilitate the discovery of molecular phenotypes linked to specific clinical expressions of mood disorders (Williams et al., 2024). Neuroimaging methods further complement these efforts by offering objective, quantifiable biomarkers of brain dysfunction that can support stratification and track treatment responses (Schumann et al., 2019; Williams & Hack, 2021).

Combining these innovations, along with the use of large and diverse cohorts, allows for stratifying patients into biologically meaningful subtypes, or “biotypes” (Chen et al., 2022b; Lee et al., 2022). For instance, several studies employing data-driven clustering approaches on neuroimaging and multi-omics data have been proven to successfully identify depression subtypes characterized by distinct clinical features and biological correlates, such as inflammatory and genetic profiles (Buch & Liston, 2021; Tang et al., 2025). These findings represent a shift from seeking universal biomarkers to identifying subtype-specific signatures, which are essential for a comprehensive understanding of mood disorders’ etiopathogenesis, as well as to implement targeted interventions (Suseelan & Pinna, 2023; Wallstrom et al., 2013).

In addition, the integration of clinical phenotyping with biological, genetic, and computational data has been suggested as a necessary approach to guide individualized therapeutic strategies (Maj et al., 2020). For example, stratifying patients based on longitudinal illness patterns or specific neurobiological profiles, as it is already partially practiced in BD treatment with lithium for mania and anticonvulsants for rapid cycling, demonstrates the clinical utility of tailoring interventions to patient subtypes (Suseelan & Pinna, 2023). In recent years, large-scale predictive modeling initiatives, such as the International Study to Predict Optimized Treatment in Depression (iSPOT-D) (Saveanu et al., 2015) and Tulsa-1000 (Victor et al., 2018) studies, show this shift by employing ML and integrating multi-dimensional data to predict treatment response. These models adopt pre-treatment variables, ranging from symptom profiles and cognitive performance to neuroimaging and genetic markers, to match patients with the interventions most likely to produce clinical benefit, even before treatment is initiated (Williams et al., 2024).

In summary, the heterogeneity of mood disorders presents significant challenges but also unique opportunities. By embracing transdiagnostic, multimodal, and highly-dimensional data, along with advanced ML technologies, both research and clinical psychiatry can move towards more precise, individualized frameworks. This paradigm shift, anchored in biological, computational, and clinical integration, has the potential to transform diagnosis, treatment, and prognosis in mood disorders, paving the way for a new era of personalized mental healthcare.

1.3 Computational approaches for patients' stratification

Given the growing awareness of the limits and challenges of the traditional psychiatric nosology, unable to capture the complex and heterogeneous nature of mood disorders, psychiatric research is undergoing a significant transformation, marked by a transition from traditional symptom-based, hypothesis-driven paradigms to data-driven approaches grounded in empirical evidence (Chen et al., 2022b). As previously mentioned, this growing awareness has given rise to the field of precision psychiatry, which seeks to identify biologically meaningful patient subtypes to enhance diagnostic accuracy, predict treatment response, and inform personalized interventions (Bzdok & Meyer-Lindenberg, 2018). A pivotal enabler of this paradigm shift is the increasing availability of big data, i.e., large-scale, multimodal datasets that include genetic, neuroimaging, behavioral, environmental, and clinical information (Reel et al., 2021). These datasets, characterized by the so-called “five V’s” of big data (i.e., volume, velocity, variety, veracity, and value), offer unprecedented opportunities to model disease processes at a fine-grained level, while also posing analytical challenges due to their high dimensionality and intrinsic noise (Lee & Yoon, 2017).

With the advent of computational psychiatry, powerful mathematical tools such as ML have been increasingly employed by researchers to handle high-dimensional data and uncover complex relationships among them. Indeed, ML can be defined as a subset of artificial intelligence that involves developing algorithms able to learn patterns from data without relying on any a priori hypothesis (Huys et al., 2016). Unlike conventional statistical models, which require theoretical assumptions about the underlying data distribution, ML methods are flexible and scalable, making them ideal for uncovering non-linear and interactive relationships in complex datasets (Ostojic et al., 2024).

Moreover, ML techniques allow for out-of-sample predictions at the individual level, thereby enabling the possibility to translate group-level inferences into clinical practice (Vieira et al., 2017).

ML algorithms are typically classified into three major categories: supervised, unsupervised, and reinforcement learning (Choi et al., 2020; Linthicum et al., 2019). Supervised learning algorithms are trained on labeled datasets and are frequently used for classification and prediction tasks, such as predicting treatment outcomes or detecting the onset of psychiatric disorders (Bzdok & Meyer-Lindenberg, 2018). In contrast, unsupervised learning algorithms are employed on unlabeled data and aim to uncover latent structures or patterns without predefined outcomes. This makes them particularly well-suited for patient stratification in heterogeneous conditions such as mood disorders, where subtypes may not be clinically apparent (Eckhardt et al., 2023). A third category, reinforcement learning, is designed for sequential decision-making tasks, with algorithms trained to improve their performance based on feedback from the environment. While less common in clinical psychiatry at present, it holds promise for adaptive treatment modeling (Choi et al., 2020; Linthicum et al., 2019).

In recent years, unsupervised learning has gained attention in psychiatric research due to its utility in exploring patients' heterogeneity, identifying novel disease subtypes, and generating hypotheses for further investigation. The following sections will therefore provide a comprehensive overview of the principles, methods, and challenges associated with unsupervised ML in the context of mood disorders' stratification.

1.3.1 Overview of unsupervised machine learning

Unsupervised ML includes thousands of clustering algorithms that vary in their essential design, assumptions, parameters, and structure of target data. Nevertheless, the most widely used in psychiatric research can be grouped into four main categories (Gao et al., 2023) (**Figure 4**): i) center-based partitioning clustering (Figure 4A), aimed at finding the center of each cluster (pre-specifying the number of clusters) and establishing group membership according to the distance to each cluster center; ii) hierarchical clustering (Figure 4B), which classifies observations into a hierarchy of clusters; iii) density-based clustering (Figure 4C), which identifies clusters of different shapes and

sizes based on the density of data; iv) model-based clustering (Figure 4D), which assumes the existence of latent partitions underlying the data distribution.

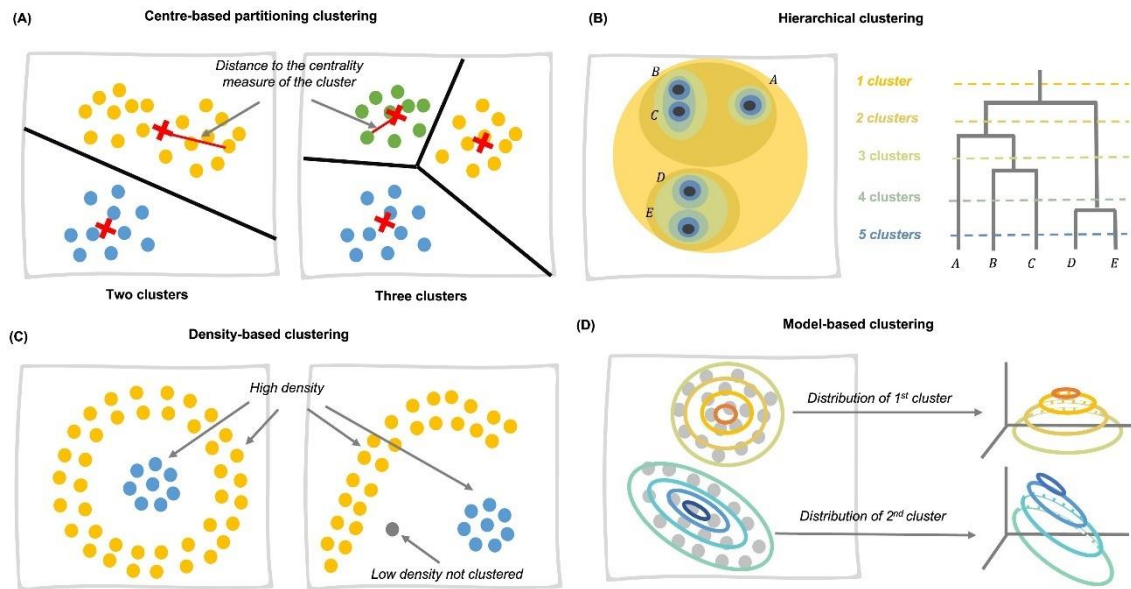


Figure 4. Graphical representation of the four main categories of unsupervised ML algorithms. Reprinted from Gao et al. (2023) (Open Access source).

Among center-based partitioning clustering methods, K-means is the most commonly adopted, especially given its ability to partition high-dimensional data into distinct groups. Specifically, K-means iteratively assigns data points to a fixed number of clusters (k) by minimizing intra-cluster variance. The algorithm begins by randomly initializing k centroids and then alternates between assigning each point to the nearest centroid and updating centroid positions based on cluster means. This process repeats until convergence (Eckhardt et al., 2023). K-means is valued for its computational efficiency and simplicity. However, it assumes that clusters are spherical and uniformly sized, which can be a limitation when applied to real-world biomedical data. It also requires prior knowledge of the number of clusters (k), which is not always straightforward to determine. Moreover, it is sensitive to both outliers and the random starting point, thereby being able only to reach the local optimum solution (Jain, 2010).

Hierarchical clustering builds a tree-like structure (i.e., dendrogram) of nested clusters without requiring the number of clusters to be specified in advance. This approach can be either agglomerative (i.e., bottom-up) or divisive (i.e., top-down), based on dissimilarity between sub-clusters (Gao et al., 2023). In the agglomerative approach,

each observation starts as a cluster, and then pairs of clusters are iteratively merged based on their similarity. The divisive strategy begins with a single cluster that recursively splits until reaching as many clusters as the number of observations. Dissimilarity is computed using linkage methods (which can be single, complete, or average), and the resulting dendrogram can be “cut” at different levels to extract a desired number of clusters (Eckhardt et al., 2023). Despite being flexible and interpretable, hierarchical clustering has some major limitations, including the computational cost on large datasets, the sensitivity to noise and outliers (i.e., low stability), and the inability to predict cluster membership among new observations (Milligan, 1980).

Density-based clustering methods do not rely on similarity or proximity of the data, but conversely identify clusters as areas of high point density separated by regions of low density, leaving unclustered those observations that are particularly distant from dense regions. The Density-Based Spatial Clustering of Applications with Noise (DBSCAN) is one of the most widely used algorithms within this family. One of its main advantages is not requiring the definition of the number of clusters in advance. Moreover, it can identify arbitrarily shaped clusters while being robust to outliers and noise (Gao et al., 2023). However, this algorithm is not able to find clusters with different densities, and it is heavily time-consuming on extensive and highly dimensional datasets (Campello et al., 2013). Furthermore, its performance greatly depends on the choice of parameters such as the neighborhood radius (*epsilon*) and the minimum number of points to be included in the clusters (*minPoints*), which are arbitrarily decided by the user (Gao et al., 2023).

Finally, model-based clustering techniques assume that the data are generated from a mixture of probability distributions. Specifically, Gaussian Mixture Models (GMMs) are the most widely used algorithms when the observed variables are continuous, since they assume that the data follow several Gaussian distributions, each corresponding to a different cluster. On the other hand, when the dataset features are discrete, the most common approach becomes the Latent Class Analysis (LCA) (Gao et al., 2023). Unlike K-means, which makes hard assignments of data points to clusters, GMMs allow for probabilistic memberships, meaning that each observation can belong to multiple clusters with varying degrees of certainty (Klem et al., 2022). This probabilistic framework makes GMMs suitable for data with overlapping or non-spherical clusters. However, they are

more computationally demanding and can be sensitive to initialization and convergence issues (Gibbons et al., 1984).

Before applying any clustering approach, critical pre-processing steps such as normalization, variable selection, and dimensionality reduction are required (Gao et al., 2023). Indeed, data utilized for clustering purposes frequently exhibit high variability and dimensionality, which pose significant challenges in terms of computational efficiency and convergence for many conventional clustering algorithms.

First, to accurately estimate similarity metrics or underlying probability distributions, it is often necessary to transform the input data to harmonize their scale, variance, and distributional skewness (Gao et al., 2023). Standard transformation techniques include z-score normalization, min-max scaling, quotient normalization, and the Box-Cox power transformation, each with distinct implications depending on the context (Jajuga & Walesiak, 2000; Milligan & Cooper, 1988). For instance, when relative differences among individuals across features are of primary interest, z-score normalization may be more effective. Conversely, if preserving the absolute magnitude of variability between features is the primary objective, min-max normalization might be more suitable due to its retention of original variable dispersion.

A frequent complication in clustering high-dimensional data arises from the inclusion of non-informative or low-quality variables that do not contribute meaningfully to the latent structures, thereby hindering the identification of true clusters (Gao et al., 2023). Hence, it is essential to undertake rigorous variable selection to retain only those features with high integrity and relevance to the latent heterogeneity under investigation. Alternatively, advanced computational techniques may be employed to manage data noise and mitigate low-quality-related issues (Shen et al., 2014).

To further enhance the effectiveness of clustering algorithms, dimensionality reduction techniques are frequently employed to project high-dimensional data into a lower-dimensional space. These transformations aim to preserve essential structural characteristics while reducing computational complexity (Gao et al., 2023). Linear methods such as principal component analysis (PCA) and factor analysis are the most widely employed approaches in psychological research contexts (Jolliffe, 2022). However, non-linear dimensionality reduction techniques – including kernel-PCA and Uniform Manifold Approximation and Projection (UMAP) – are increasingly being used,

given their ability to capture complex interdependencies and non-linear relationships among variables (Cunningham & Ghahramani, 2015).

Finally, evaluating the quality of clusters derived from unsupervised ML is crucial to ensure that the algorithms produce meaningful and useful results. This process typically involves a combination of quantitative measures and qualitative assessments.

Quantitative evaluation metrics are generally categorized into three main types (Gan et al., 2020): external validation indices, which assess the extent to which the clustering solution aligns with pre-existing or known class labels (i.e., ground truth); internal validation indices, which measure the coherence and separation of clusters based solely on the intrinsic properties of the data; and relative validation criteria, which are used to compare the performance of different unsupervised algorithms or parameter configurations to determine the optimal clustering solution.

The most commonly used quantitative metrics include Silhouette score, Davies-Bouldin index, and Calinski-Harabasz index (Halkidi et al., 2001; Liu et al., 2013). The Silhouette score (Rousseeuw, 1987) measures how similar an observation is to its cluster (i.e., cohesion) compared to other clusters (i.e., separation). Values range from -1 to 1, where a higher value indicates better-defined clusters, meaning that data points are well-matched to their cluster and poorly matched to neighboring clusters. The Davies-Bouldin index (Davies & Bouldin, 2009) evaluates clustering performance based on the ratio of within-cluster to between-cluster distances. Lower values indicate better clustering, with a value of 0 signifying well-separated and compact clusters. Finally, the Calinski-Harabasz index (Caliński & Harabasz, 1974), similarly to the Davis-Bouldin, assesses the ratio of between-cluster to within-cluster variance.

In addition to quantitative metrics, visual inspection of data distribution remains an important tool for evaluating the separation and cohesion of clusters. However, this approach becomes increasingly challenging for high-dimensional datasets, where visualizations such as scatterplots may hide complex multivariate patterns due to overlap and clutter (Liao et al., 2017). As a result, effective assessment of cluster quality in psychiatric patient stratification requires a comprehensive strategy that integrates both quantitative internal indices (e.g., Silhouette, Davies-Bouldin) and qualitative evaluations (e.g., visualization, clinical interpretability). Moreover, while quantitative metrics offer objective assessments of structural properties within the data, they alone are insufficient

to determine the clinical or biological relevance of identified clusters. Expert domain knowledge is therefore essential for interpreting the practical significance of data-driven subtypes and ensuring their real-world applicability (Gao et al., 2023). Ultimately, the validation of stratification approaches in psychiatry must prioritize not only algorithmic performance but also clinical and biological interpretability. Statistically sound clusters yet lacking meaningful external correlates (e.g., in terms of treatment outcomes, genetic markers, or neurobiological features) provide limited translational value. Hence, external validation against such criteria is critical to establish the utility of derived subgroups as clinically actionable or biologically distinct entities (Marquand et al., 2016).

1.3.2 Emerging evidence in mood disorders research

In recent years, given the suitability of clustering algorithms to find homogeneous subgroups of observations, unsupervised ML has emerged as a powerful tool to disentangle heterogeneity in mood disorders, moving beyond traditional symptom-based classifications to identify latent subgroups or biotypes of MDD and BD. This data-driven shift aligns with a broader movement in psychiatry to uncover the mechanistic underpinnings of mental disorders, leveraging complex datasets encompassing clinical symptoms, neuroimaging data, genetics, and other biomarkers (Beijers et al., 2019; Marquand et al., 2016). The most commonly employed clustering techniques in this field include K-means, hierarchical clustering, GMMs, and LCA. Remarkably, many of the resulting clusters have demonstrated meaningful associations with clinical outcomes, including disease course, treatment response, and functional impairment.

Early applications of unsupervised ML in mood disorders primarily focused on dissecting the heterogeneity within MDD based on clinical symptom profiles. These studies laid the foundational groundwork by empirically deriving subtypes that often transcended the limitations of existing diagnostic criteria. A pioneering work by Kendler et al. (1996) utilized LCA on 14 DSM-III-R symptoms in a population-based sample of 1029 female twin pairs, identifying seven latent classes, three of which represented clinically significant depressive syndromes: mild typical depression, atypical depression, and severe typical depression. The severe typical subtype was characterized by significant comorbidity with anxiety and panic disorders, prolonged episodes, substantial functional impairment, and a higher likelihood of seeking professional help. In contrast, the atypical

subtype, while similar in severity to mild typical depression, presented with distinctive features such as increased appetite, weight gain, hypersomnia, and frequent, relatively short episodes. These findings were subsequently replicated and extended by Sullivan et al. (1998) in a larger epidemiological sample from the National Comorbidity Survey, involving 2,836 subjects. Applying LCA to lifetime major depressive symptoms, they identified an optimal six-class solution, with four of these classes representing combinations of typical-atypical depression and severity (i.e., severe atypical, mild atypical, severe typical, and mild typical depression), replicating the associations found in their previous study between severity, atypical symptoms, and worse clinical profiles.

Further refining symptom-based stratification, Lamers et al. (2010) conducted a study within the Netherlands Study of Depression and Anxiety (NESDA) cohort, involving 818 individuals with current DSM-IV major or minor depression. Using LCA on 16 depressive symptoms, they identified three distinct classes: a severe melancholic class (46.3% prevalence), a severe atypical class (24.6% prevalence), and a moderate severity class (29.1% prevalence). Both severe classes were characterized by elevated neuroticism, greater disability, and reduced extraversion compared to the moderate class. The melancholic subtype showed higher rates of smoking and childhood trauma, whereas the atypical subtype was more prevalent in women and exhibited a higher body mass index (BMI) and a significantly greater prevalence of metabolic syndrome, thereby suggesting a metabolic component underlying atypical depression. The generalizability of these symptom-based subtypes across different age groups was subsequently explored by Lamers et al. (2012), who applied LCA to 12-month MDD in nationally representative samples of 912 US adolescents and 805 adults. On this occasion, the authors found three subtypes in adolescents and four in adults, with a severe typical subtype and an atypical subtype being consistent across both age groups. The atypical subtype in both populations was consistently characterized by increased appetite and weight gain, reinforcing its distinct clinical presentation.

Building on the clinical stratification, Milaneschi et al. (2016) delved into the polygenic features of typical and atypical MDD using Genomic Profile Risk Scores (GPRS) in a large sample from NESDA and the Netherlands Twin Register (including 1530 MDD patients and 1700 healthy controls). The study found that while MDD was generally associated with psychiatric GPRS, its subtypes exhibited differential polygenic

signatures, with typical depression showing a strong association with SCZ GPRS, and atypical depression being linked to GPRS for BMI and triglycerides. Moreover, each distinct subtype exhibited different rates of SNP-heritability, suggesting that these empirically derived subtypes represented more genetically homogeneous phenotypes with distinct polygenic liabilities.

More recently, Wang et al. (2025) utilized Latent Profile Analysis (LPA) to identify five distinct MDD subtypes based on validated clinical symptoms in a cross-sectional study of 259 MDD patients and 92 healthy controls. The optimal five-class model revealed an atypical-like depression subtype, two melancholic depression subtypes (i.e., moderate and severe) with differing patterns of anxiety, and two anhedonic depression subtypes (also moderate and severe) with varied manifestations of weight/appetite loss. Importantly, these identified subtypes also exhibited significant differential neural activities, both in regional spontaneous neural activity and functional connectivity between brain regions, which were linked to their specific clinical symptoms. In line with these findings, Maglanoc et al. (2019) also performed a symptom-based clustering in a large transdiagnostic cohort, including 1084 individuals with or without depression history, using Beck Depression and Beck Anxiety Inventories, and then assessing brain functional connectivity correlates in a subset of 252 subjects. Similarly to Wang et al. (2025), the study also identified five subgroups with distinct symptom profiles that cut across traditional diagnostic boundaries. These subgroups showed differential brain-connectivity patterns, particularly involving a frontotemporal network, suggesting that specific symptom combinations were linked to distinct neural substrates. This multi-modal validation reinforces the idea that data-driven symptom clusters are not arbitrary but reflect true biological distinctions. This is a critical step in building a more robust and clinically useful nosology for mood disorders, as it moves beyond purely observable phenomena to incorporate etiological and mechanistic insights.

All these symptom-based clustering applications can be described as “top-down” approaches, subtyping patients based on their clinical phenotype and then investigating the neurobiological underpinnings of the identified clusters, in contrast to the most recent and emerging “bottom-up” brain-based mechanistic strategies (Buch & Liston, 2021). The latter approach was first adopted by two early studies of Price and colleagues (2017a, 2017b), who explored resting-state connectivity-driven subtypes of depression. In their

first study, using Group Iterative Multiple Model Estimation (GIMME) to derive rsFC paths in 80 depressed patients, two distinct subgroups were identified. While one cluster exhibited a typical DMN hyperconnectivity pattern, the other one showed an atypical profile lacking DMN connectivity, along with increased dorsal anterior cingulate-driven activity. Additionally, the second subgroup was significantly associated with a higher proportion of females, comorbid anxiety diagnoses, and highly recurrent depression (Price et al., 2017a). Their second study extended these findings by applying the same methodology to 92 individuals, including 68 MDD and 24 controls (Price et al., 2017b). Two connectivity-based subgroups were again uncovered, one characterized by weaker overall connectivity and another exhibiting hyperconnectivity, especially in ventral affective regions. The second subgroup included 81% of patients and was associated with higher self-reported symptoms, lower sustained positive mood, and negative bias. The identification of symptom subgroups that “cut across diagnostic boundaries” suggests that the underlying biological and symptomatic dimensions might not neatly align with current diagnostic categories. These findings hence reinforce the idea that mental disorders might be better understood as dimensional constructs or as collections of transdiagnostic biotypes rather than discrete categories, which has profound implications for diagnosis and treatment.

A landmark study of this “bottom-up” clustering approach was performed by Drysdale et al. (2017), who utilized rs-fMRI data of 1,188 patients with MDD and identified four biotypes characterized by distinct patterns of dysfunctional connectivity within limbic and fronto-striatal networks. Moreover, these biotypes were associated with differing clinical-symptom profiles and significantly predicted responsiveness to TMS therapy, suggesting a path toward identifying individuals most likely to benefit from targeted neurostimulation. However, the robustness and generalizability of these findings were questioned by Dinga et al. (2019), who attempted a methodological replication in a different, more heterogeneous sample of 187 participants with depression and anxiety. While they found extremely high canonical correlations between functional connectivity and clinical symptoms and an optimal three-cluster solution, neither the canonical correlations nor the identified clusters were statistically significant. Based on extensive evaluations and resampling analyses, the authors argued that the evidence for the existence of distinct resting-state connectivity-based subtypes of depression should be

interpreted with caution. This highlights a critical challenge in the field, that is, ensuring that identified clusters represent true biological distinctions rather than statistical artifacts. In response to these concerns, Grosenick et al. (2019) further investigated the stability of canonical correlations between functional connectivity and symptoms among 220 subjects, highlighting that while correlations were robustly significant and generalized to held-out data, they were sensitive to data quality, preprocessing, and clinical heterogeneity, which could diminish effect sizes. Crucially, the authors demonstrated that adding L_2 regularization markedly improved generalization by stabilizing feature selection, thereby underscoring the importance of methodological rigor and external validation. Therefore, for computational stratification to move from research to clinical practice, identified biotypes must be consistently reproducible across different datasets and validated using robust statistical methods. This calls for community-wide standards for data sharing, preprocessing pipelines, and validation metrics to build confidence in the derived subtypes (Miranda et al., 2021).

Beyond depression stratification on fMRI data, some studies have also attempted to identify data-driven biotypes based on structural neuroimaging. For instance, Cheng et al. (2014) utilized DTI data on 61 pairs of untreated, first-episode MDD patients and healthy controls, and identified two distinct subgroups of late-onset and early-onset disease. The late-onset cluster of patients was characterized by significantly decreased FA, particularly in the fronto-occipital fasciculus and posterior limb of the internal capsule, negatively correlating with symptom severity. In contrast, the early-onset cluster showed increased FA, especially in the corpus callosum, corticospinal midbrain, and inferior fronto-occipital fasciculus, with FA near the midbrain positively correlating with symptom severity. A more recent study by Colombo et al. (2024) employed a stability-based relative clustering validation ML approach to stratify 102 MDD patients based on multimodal structural MRI, including cortical thickness, GM volume, and FA. Two neurobiologically distinct clusters emerged with a classification accuracy of 67%, with one subgroup being marked by more severe clinical features, including TRD, higher levels of fatigue-related symptoms, and greater exposure to childhood trauma. The same group also showed widespread reductions in cortical thickness and volume, and lower white matter integrity in specific tracts (e.g., fronto-occipital fasciculus, stria terminalis, corpus callosum). Conversely, the other cluster exhibited more cognitive and emotional

symptoms, along with generally thicker cortices and larger brain volumes. Importantly, subsequent multivariate analysis highlighted distinct relationships between neuroanatomy and peripheral inflammation across the two subtypes, with pro-inflammatory markers correlating with structural brain reductions in the more clinically severe group. These findings are in line with a subsequent study by Tang et al. (2025), which integrated a functional neuroimaging-based stratification with multi-omics data. Indeed, in a study of 327 MDD patients and 480 healthy controls, using ALFF extracted measures, the authors identified three MDD subtypes, each with unique ALFF pattern alterations. Multi-omics analysis, including genetics, epigenetics, metabolomics, and pro-inflammatory cytokines, revealed distinct biological underpinnings for two of these subtypes. While subtype 1 showed a strong genetic predisposition enriched in neuronal development and synaptic regulation pathways, correlating with the most severe depressive symptoms and cognitive decline, subtype 2 was characterized by immuno-inflammatory dysregulation, evidenced by elevated interleukin-1 β (IL-1 β), altered epigenetic inflammatory measures, and levels of metabolites. These findings provide examples of neurobiologically-informed and clinically relevant stratification of depression, providing insights for future mechanism-targeted therapies. In addition to these studies, a previous research by Tokuda et al. (2018) also adopted a multimodal data-driven approach to identify neurophysiological subtypes of depression. Specifically, the authors enrolled 134 individuals, including 67 with MDD and 67 healthy controls, and integrated rsFC, clinical questionnaires investigating depression severity, personality traits, and early-life stress, and biological markers such as BDNF levels, cortisol, SNPs, and DNA methylation. By applying a co-clustering method, which simultaneously partitions both subjects and features, three distinct subtypes of depression (i.e., D1, D2, D3) were identified. Remarkably, each cluster was defined by unique combinations of ACC connectivity and childhood trauma history and differentially predicted remission or resistance to SSRI antidepressant therapy. For instance, individuals in D3, marked by lower ACC connectivity, tended to have better treatment responses; subjects in D1, with higher rates of childhood trauma, displayed poorer remission outcomes; those with both high ACC connectivity and lower trauma scores, belonging to D2, exhibited more favorable SSRI responses.

Taken together, these studies demonstrate the power of integrating diverse data types, moving beyond simply identifying brain patterns to linking them with genetic predispositions, inflammatory markers, and clinical severity, and directly linking multi-modal subtypes to treatment response. This is a significant step over descriptive clustering and highlights the future direction of computational psychiatry, that is, building comprehensive biological profiles for individuals by combining data from multiple levels of analysis (Beijers et al., 2019; Miranda et al., 2021).

While unsupervised ML approaches have been widely employed to stratify MDD patients, fewer studies have applied these methods to BD and the broader psychosis spectrum, revealing distinct cognitive, longitudinal, and cross-diagnostic subtypes. Considering the BD population alone, only two studies conducted by the ENIGMA consortium employed brain structure measures to cluster patients with bipolar disorders. For instance, McWhinney et al. (2023) stratified 836 patients with BD and 1,600 healthy controls using regional cortical thickness and surface area measures. Specifically, employing a K-means clustering, the authors identified two distinct clusters based on cortical thickness, with one cluster significantly showing thinner frontal and temporal cortices, higher BD cases, increased BMI, and older age. By contrast, the clustering solution obtained by exploiting only surface area measures uncovered significant differences only for age and sex, without any significant association with diagnosis or BMI (McWhinney et al., 2022). In a subsequent study of the same group, PCA was employed to examine patterns of cortical morphology in 2,436 individuals with BD and controls (McWhinney et al., 2024). The first principal component, reflecting widespread cortical thickness, was negatively associated with BD diagnosis, higher BMI, older age, and antipsychotic medication use, while positively related to lithium treatment. When directly compared to the previous clustering analyses, PCA provided a superior fit in capturing associations with diagnosis and BMI. Crucially, the model was validated in an independent replication sample of 327 participants, including BD, schizophrenia, and controls, where the same cortical thickness component differentiated patients from healthy individuals and showed consistent links with clinical and demographic measures, including diagnosis, age, BMI, and treatment with antipsychotic medications or lithium. Other stratification analyses involving BD patients adopted transdiagnostic approaches. For instance, Lewandowski et al. (2014) applied a clustering analysis to cognitive profiles

in a cross-diagnostic sample of 167 patients with psychotic disorders, including SCZ, schizoaffective disorder, and BD with psychosis. Using Ward's method followed by K-means, a four-cluster solution was identified, with a neuropsychologically preserved cluster, a globally and significantly impaired cluster, and two clusters with mixed cognitive profiles. Importantly, while these clusters differed on several clinical variables, diagnoses were distributed across all clusters, suggesting that cognitive impairment might represent a transdiagnostic dimension rather than being strictly tied to a single diagnostic category. Kleinman et al. (2015) also conducted a transdiagnostic stratification by using pattern recognition on Conners' Continuous Performance Test (CPT II) data in 84 youth with BD, ADHD, BD+ADHD, and healthy controls. The clustering analysis yielded two attention-based groups that cut across the original diagnoses, with one group exhibiting greater impairment across all CPT II variables and lower global functioning. More recently, Dwyer et al. (2020), in the large multi-site PsyCourse study, applied non-negative matrix factorization (NMF) clustering to a clinical battery of 188 variables in 1,223 individuals with various DSM-IV psychosis diagnoses, including BD. The study identified five robust psychosis subgroups: affective psychosis, suicidal psychosis, depressive psychosis, high-functioning psychosis, and severe psychosis. These subtypes exhibited distinct illness courses over 1.5 years, with the depressive and severe psychosis subgroups showing the lowest functioning and a pattern of partial recovery followed by reoccurrence of severe illness. Differences were also found for educational attainment PGSs, but not for diagnostic PGSs, with results largely replicated in a validation cohort. This study hence provides strong evidence for data-driven psychosis subgroups with prognostic and genetic validation, extending the utility of ML beyond MDD. The collective evidence suggests that data-driven approaches are revealing underlying dimensions of psychopathology (e.g., cognitive impairment, attentional deficits, specific illness trajectories) that are shared across disorders. This further supports a move towards a more dimensional or transdiagnostic classification system, potentially leading to more effective, mechanism-based treatments for patients currently categorized under broad, heterogeneous diagnostic labels.

1.3.3 Strengths and pitfalls of current stratification approaches

As highlighted in the previous section, unsupervised ML has become a key tool to disentangle the clinical and biological heterogeneity that characterizes mood disorders. The data-driven nature of these approaches is one of their main strengths. Indeed, unsupervised ML does not depend on predefined diagnostic labels, allowing it to identify latent subgroups based on complex, high-dimensional data from clinical, neuroimaging, genetic, and other biological sources. This capability has resulted in subtypes that are not only statistically solid but also clinically and biologically meaningful. For example, structural neuroimaging subtypes identified by Colombo et al. (2024) showed different rates of TRD along with distinct inflammatory profiles, while Milaneschi et al. (2016) showed that distinct genetic and metabolic profiles characterized atypical depression subtypes. These findings underscore the potential of these methods for creating more targeted and effective treatments, thereby promoting precision psychiatry.

Additionally, unsupervised ML facilitates the exploration of multimodal data integration, a critical advantage given the multifactorial etiology of mood disorders. Studies such as Tang et al. (2025) and Tokuda et al. (2018) have shown the value of integrating neuroimaging, genetic, and epigenetic markers to derive biologically-informed subtypes with unique mechanistic underpinnings.

Another advantage of unsupervised ML techniques is the possibility to identify cross-diagnostic or transdiagnostic constructs, providing an empirical foundation to revise or extend the existing psychiatric nosology. Moreover, recent methodological developments, such as regularized canonical correlation analysis, have improved the interpretability and reproducibility of unsupervised findings (Grosenick et al., 2019).

Nevertheless, the current application of unsupervised ML in psychiatry presents several critical limitations. For example, to date, multimodal approaches are still poorly employed in the literature, with most research studies focusing on single sources of information, hence missing the complex interaction between different levels of etiopathogenetic mechanisms.

A major concern regarding unsupervised techniques is the lack of a “ground truth” for psychiatric constructs, which renders critical the evaluation of clustering solutions. Indeed, algorithms will produce clusters even when no meaningful underlying structures exist, thus highlighting the need for testing the null hypothesis that the identified clusters

are not present in the data (Beijers et al., 2019). Moreover, clusters must be validated to confirm that they are both reliable and reflect meaningful clinical differences. Indeed, statistical techniques such as resampling-based stability metrics (e.g., cross-validation, bootstrap, hold-out validation) are robust strategies to ensure reproducibility of results (Marquand et al., 2016). Yet many studies fail to conduct adequate assessments of cluster stability, internal consistency, or external generalizability, with both internal and external validation metrics often being omitted or inconsistently applied (Miranda et al., 2021).

Replication in independent datasets, i.e., out-of-sample validation, is similarly rare, limiting the translational relevance of many proposed subtypes. For example, while the biotypes detected by Drysdale et al. (2017) initially seemed promising, subsequent attempts at replication yielded less conclusive results (Dinga et al., 2019), emphasizing the need for robust methodological pipelines. Moreover, the numerosity of samples of the majority of studies employing clustering approaches on mood disorders was limited (Rajput et al., 2023), further hampering the generalizability of findings.

Another limitation pertains to the frequent use of cross-sectional data. While clustering can reveal static subtypes, it often fails to capture the dynamic nature of mood disorders. Indeed, longitudinal approaches, such as latent class growth analysis, can model symptom trajectories over time (Rhebergen et al., 2012), but are underutilized.

Additionally, many ML models are sensitive to preprocessing decisions, choice of input features, and assumptions about cluster shape or number. These arbitrary decisions can substantially influence outcomes, yet are rarely tested through sensitivity analyses or reported in full transparency (Beijers et al., 2019).

Looking ahead, future directions in this field must emphasize methodological rigor, transparency, and reproducibility. Standardizing preprocessing pipelines, feature selection criteria, and validation metrics is critical to ensure reproducibility and comparability across studies. Integration of “omics” data with neuroimaging and clinical phenotypes represents a promising frontier for mapping the biological architecture of mood disorders. Furthermore, recent work suggests that stratification approaches could benefit from hybrid models that combine supervised and unsupervised techniques (Marquand et al., 2016), enabling subtypes to be both data-driven and clinically anchored (e.g., guided by treatment response or functional outcomes).

2. Aims of the current project

As outlined in the previous chapter, mood disorders are clinically and biologically heterogeneous conditions, with patients significantly differing in their symptom profiles, underlying neurobiology, genetic liability, and exposure to environmental risk factors. This heterogeneity has long challenged our understanding of depression, hindering the identification of reliable biomarkers and limiting the effectiveness of existing treatments, thereby slowing the development of targeted and effective interventions. Indeed, the high variability across clinical trajectories, treatment responses, and health outcomes underscores an urgent need for objective markers that can help disentangle this heterogeneity and identify depression subtypes that may benefit from distinct and tailored treatment strategies. Recent advances in computational psychiatry have created novel opportunities to classify patient subgroups based on shared characteristics. However, most studies focused on a single source of heterogeneity (e.g., brain morphology or function alone), overlooking the complex interactions among multiple pathophysiological mechanisms, and lacked external validation strategies. In light of this background, the current project aimed to identify distinct biologically and clinically meaningful subtypes of depression, addressing these challenges and filling these critical gaps in current research frameworks. To this end, advanced computational methods were applied to two deeply phenotyped, large-scale cohorts, integrating multimodal neurobiological and environmental information to unravel the interplay of etiopathological mechanisms contributing to the variability in mood disorders.

The primary analyses of this project were conducted on a wide cohort of over 3,500 individuals with a history of MDD from the UK Biobank (UKB). To ensure the generalizability of findings, the results were replicated in an external cohort of thoroughly phenotyped MDD patients recruited at the IRCCS Ospedale San Raffaele (OSR) in Milan, Italy. Given the differences in recruitment settings (i.e., general population in UKB vs. hospitalized patients at OSR), subgroup analyses on currently depressed individuals within the UKB were also performed. Furthermore, to explore the transdiagnostic applicability of findings, analyses were extended to a sample from the OSR cohort that included both depressed MDD and BD patients, a clinical population underrepresented in the UKB (Zhao et al., 2023), possibly due to a selection bias affecting population-based cohorts (Krantz et al., 2023).

Multimodal data exploited to stratify individuals with mood disorders included genetic information, brain structure and function, and environmental risk factors, as all these features have been shown to contribute to the heterogeneity of depression. Specifically, genetic data consisted of several PGSs for psychiatric conditions, relevant medical comorbidities, and inflammatory markers (Mitchell et al., 2025). Structural and functional neuroimaging measures encompassed GM volume, cortical thickness, surface area (Schmaal et al., 2017), white matter diffusivity indices (van Velzen et al., 2020), positive and negative strength of resting-state networks (Javaheripour et al., 2021; Kaiser et al., 2015b), and mean activation and amygdala habituation measures during an implicit emotion processing task (Pilmeyer et al., 2022; Vai et al., 2023). Finally, environmental stressors included both ACEs and adult SLEs (Park et al., 2019). All these features were first employed in separate unimodal stratification models, and secondly combined into a single multimodal model, joining those data that allowed for a significant clustering solution. This step enabled us to assess whether the integration of multiple sources of heterogeneity would enhance the identification of biologically meaningful and homogeneous subtypes of depression. Moreover, given the high dimensionality and collinearity of the utilized data, especially of the neuroimaging-derived measures (Gao et al., 2023), a PCA on each modality was computed to conduct, as a supplementary analysis, stratification models on the dimensionally-reduced datasets.

As regards statistical analyses, a novel and sophisticated unsupervised ML pipeline, specifically designed to define stable clustering solutions, was employed. In particular, a consensus clustering approach – as originally designed by Monti et al. (2003) – was adopted, consisting of an ensemble strategy that condenses multiple clustering repetitions into a single, robust solution. The analysis was iterated for different possible numbers of clusters, thereby allowing for the selection of the optimal clustering solution based on the agreement of internal validation metrics. The consistency and significance of the identified clusters were rigorously validated using additional external metrics, ensuring they represented truly distinct underlying distributions emerging from the data, rather than statistical artifacts. Once identified, the data-driven depression subtypes were thoroughly characterized in terms of their clinical features, including cardiometabolic comorbidities, treatment resistance, self-harming behaviors, and cognitive performance. This step was crucial for determining the clinical relevance of the defined clusters,

assessing whether they corresponded to meaningful differences and distinct presentations of the depression phenotype. Finally, to evaluate the predictive utility and potential translational application of the identified clusters, supervised ML models were trained to predict cluster membership and forecast important health outcomes, such as treatment resistance, comorbid diabetes or cardiovascular disease, and suicidality. These models would help determine whether the subtypes identified through an unsupervised stratification approach can support clinical decision-making and improve outcome prediction in real-world settings.

In conclusion, this project aimed to bridge clinical and computational perspectives to capture the multifaceted nature of depression and dissect its complex heterogeneity. By integrating large-scale, multimodal data with robust analytical methods, this study aimed to overcome and push forward current stratification approaches, which have mainly relied on single sources of heterogeneity, often failed to replicate results, lacked rigorous internal and external validity assessments, and demonstrated poor applicability in clinical practice. Therefore, this research work had the ultimate goal to lay the groundwork for future stratified and biologically informed diagnostic approaches to depressive disorders, fostering translational advances that can inform and optimize personalized treatment interventions.

3. Materials and methods

3.1 Participants

Two different cohorts of mood disorders were included in the current study, one retrieved from the UKB ($n=3,887$) and the other recruited at OSR ($n=475$). The UKB represents a large-scale prospective cohort study encompassing more than 500,000 individuals recruited between 2006 and 2010 from various regions across the United Kingdom, excluding Northern Ireland, with participants aged 40 to 69 years at the time of enrollment (Allen et al., 2012). This cohort has been systematically followed over time, with extensive data collection spanning clinical history, environmental exposures, lifestyle behaviors, multimodal imaging, genetic profiles, and several other biological markers. Specifically, the UKB offers detailed, longitudinal documentation of health-related outcomes and lifetime risk factors. All these variables have been collected through a combination of sources, including electronic health records (encompassing both hospital and general practitioner data) and self-reported measures. The latter were obtained via touchscreen-based questionnaires administered at baseline and through online follow-up surveys distributed over time (Conroy et al., 2019).

Consistently with a previous study stratifying depression in UKB (Fabbri et al., 2022), among all participants, individuals with lifetime MDD were identified as those meeting at least one of the following criteria: 1) having five or more depressive symptoms as assessed by the Composite International Diagnostic Interview, Short Form (CIDI-SF) (Davis et al., 2020); 2) presence of MDD-related diagnostic codes according to the ICD-10 classification (i.e., codes F32–F33); 3) documentation of at least one diagnostic entry for depressive disorders in primary care medical records (Fabbri et al., 2021); 4) fulfillment of the diagnostic criteria previously defined by Smith et al. (2013). Given that minimal phenotyping of MDD in UKB has been shown to select individuals with broader and more heterogeneous characteristics compared to more stringent phenotyping (Cai et al., 2020), measures of self-reported depression based on single-item responses were not considered (e.g., Field IDs: 2090, 2100, and 20002). Among the identified individuals with lifetime MDD, participants without any data availability for multimodal neuroimaging, genetics, and stress-related data, as well as those aged more than 65 years old at the time of MRI acquisition, and with lifetime BD, psychotic, or substance use

disorders (according to either the CIDI-SF, ICD-10 codes, or primary care records) were excluded. Given these inclusion and exclusion criteria, and selecting only individuals with the availability of all types of data subsequently exploited in the stratification analysis (i.e., GM, DTI, rs-fMRI, t-fMRI, PGSs, and stress-related data), the UKB sample included in this study ultimately consisted of 3,887 individuals with lifetime MDD. Among these, a subsample of 279 subjects was identified as being currently depressed at the time of MRI scanning. Indeed, two of the self-reported measures of mental health included in the UKB are the PHQ-9 (Kroenke et al., 2001) and the Recent Depressive Symptoms (RDS-4) (Dutt et al., 2022). PHQ-9 is a nine-item questionnaire (Field IDs: 20507, 20508, 20510, 20511, 20513, 20514, 20517, 20518, 20519) that scores each of the nine DSM-IV criteria for depression as 0=“not at all” to 3=“nearly every day”. Scores range from 0-27, and a score of 15 or higher can be used as a cut-off for moderately severe depressive symptomatology (Kroenke et al., 2001). Conversely, RDS-4 is a measure of depression symptomatology that uses four self-report questions to evaluate depressed mood, disinterest, restlessness, and tiredness (Field IDs: 2050, 2060, 2070, 2080). These questions inquire about symptoms experienced in the past two weeks and, unlike the PHQ-9 that was administered at the time of enrollment, the RDS-4 was completed on the same day as the imaging scan. The response options range from 1=“not at all” to 4=“nearly every day”, with the total score from these questions spanning from 4 to 16. Notably, a score of 10 on this scale has been mapped to the PHQ-9 threshold for moderately severe depression (Dutt et al., 2022), and therefore, it was used in the present study to select the subsample of currently depressed individuals at the time of MRI acquisition.

The OSR sample comprised a total of 475 hospitalized patients, including 211 with MDD and 264 with BD, aged between 18 and 65 years. The assessment of both diagnoses was made according to the DSM-5 criteria, specifically using the Italian translation of the Structured Clinical Interview for the Diagnosis of DSM-5 Disorders, Clinical Version (SCID-5-CV) (First et al., 2015). All patients were currently experiencing a major depressive episode, as assessed by a minimum score of 8 at the 21-item version of the HAM-D scale (Hamilton, 1960). To be eligible for recruitment into the study, participants must not have had a history of intellectual disability, major medical or neurological disorders, substance use disorder, or be pregnant. Before participating in the study, all

participants provided written informed consent after being informed about the research objectives and the procedures that ensured data anonymity. The study protocol, including all clinical and research methods, received approval from a local Ethics Committee of the IRCCS Ospedale San Raffaele. All aspects of the investigation were conducted in full compliance with the ethical guidelines set forth by national and institutional committees on human experimentation, as well as the principles outlined in the World Medical Association's Declaration of Helsinki (1975), as amended in 2013.

3.2 Neuroimaging data

In UKB, multimodal MRI data have been collected from approximately 85,000 participants and have already been pre-processed to generate several imaging-derived phenotypes (IDPs), including measures extracted from T1-weighted images, DTI, rs-fMRI, and t-fMRI. These IDPs were produced by the image-processing and quality control (QC) pipeline developed and operated on behalf of the UKB (Alfaro-Almagro et al., 2018). This pipeline is a robust processing protocol mainly based on FMRIB's Software Library (FSL) (Jenkinson et al., 2012), enabling integration across various structural and functional MRI modalities. It was designed to provide a standardized protocol accessible to all neuroimaging researchers, similar to the approaches adopted by the Human Connectome Project (HCP) (Glasser et al., 2013) or the ENIGMA processing pipelines (ENIGMA, 2025). Consequently, neuroimaging data from the OSR cohort were also pre-processed according to this protocol to minimize potential confounding effects between cohorts, further supporting the reproducibility and comparability of results. A detailed overview of the UKB acquisition parameters, image pre-processing, and QC procedures is available elsewhere (Smith et al., 2024) and is summarized in the following sections. The complete list of IDPs included in the clustering analyses is provided in the **Appendix Table A1**.

3.2.1 Acquisition parameters and t-fMRI paradigm

MRI data of UKB participants were acquired using a Siemens Skyra 3T scanner (Siemens Healthcare, Erlangen, Germany) with a standard 32-channel head coil, according to a freely available protocol (UK Biobank, 2014). High-resolution T1-

weighted structural images were acquired using a 3D MPRAGE sequence with the following parameters: repetition time (TR) = 2000 ms, inversion time (TI) = 880 ms, matrix size = 256×256 , 208 sagittal slices, voxel dimensions = $1.0 \times 1.0 \times 1.0 \text{ mm}^3$, and an acceleration factor $R = 2$. The total acquisition time for the T1 sequence was 4 minutes and 54 seconds. DTI data were collected using a multiband (MB) factor of 3 and a spin-echo EPI sequence with TR = 3600 ms and TE = 92 ms. The acquisition included 104 slices with isotropic voxels of $2.0 \times 2.0 \times 2.0 \text{ mm}^3$, matrix size = $104 \times 104 \times 72$, and phase-encoding in both anterior-posterior and posterior-anterior directions. Diffusion weighting was applied using b-values of 0 (5 volumes + 3 reversed phase-encoding), 1000 (50 directions), and 2000 s/mm^2 (50 directions). Partial Fourier factor was 6/8, with no in-plane acceleration ($R = 1$). The total duration of DTI scanning was 7 minutes and 8 seconds. Scans for rs-fMRI were obtained using a gradient-echo EPI sequence with TR = 735 ms, TE = 39 ms, flip angle = 52° , MB = 8, $R = 1$, and fat saturation, reaching a total of 490 volumes. The voxel size was $2.4 \times 2.4 \times 2.4 \text{ mm}^3$, with a matrix of 88×88 and 64 axial slices. The total rs-fMRI acquisition lasted 6 minutes and 10 seconds. Finally, t-fMRI images were acquired with identical imaging parameters to rs-fMRI (i.e., TR = 735 ms, TE = 39 ms, voxel size = $2.4 \times 2.4 \times 2.4 \text{ mm}^3$, MB = 8, flip angle = 52°), during an implicit emotion recognition paradigm (Hariri et al., 2002). The task included two experimental conditions, namely shapes and faces, consisting of five blocks each. During each block, the displayed pictures consisted of two faces (representing angry or fearful expressions) or geometrical shapes presented in the lower part of the screen and one face/shape in the upper part. Participants were instructed to press a button to indicate which of the two images shown at the bottom matched the one presented at the top. The total acquisition time was 4 minutes and 13 seconds, yielding 332 volumes.

MRI data acquisition in the OSR cohort was performed with two distinct Philips 3T scanners. A total of 200 patients (53 with MDD, 147 with BD) were scanned using a Philips Gyroscan Intera (Philips, Netherlands) system with an 8-channel SENSE head coil. High-resolution T1-weighted anatomical scans were acquired using a 3D MPRAGE sequence with the following parameters: TR = 25 ms, TE = 4.6 ms, field of view (FOV) = 230 mm, in-plane resolution = $0.9 \times 0.9 \text{ mm}^2$, matrix = 256×256 , producing 220 axial slices with a slice thickness of 0.8 mm. Among 161 patients (48 with MDD, 113 with BD), DTI acquisition was performed using single-shot spin-echo echo-planar imaging

(SE-EPI) sequences with TR = 9000 ms and TE = 58 ms. The FOV was 232 mm (anterior-posterior) $\times$ 126 mm (foot-head) $\times$ 240 mm (right-left), and the acquisition matrix was 112×85 . The resulting voxel size was $2.14 \times 2.73 \times 2.3 \text{ mm}^3$, with 55 contiguous slices reconstructed to an in-plane resolution of $1.88 \times 1.88 \text{ mm}^2$. Diffusion gradients were applied in 35 non-collinear directions with a b-value of 900 s/mm^2 , along with one b0 image. SENSE acceleration factor was 2. Resting-state fMRI images were collected from a subset of 41 participants (17 MDD, 24 BD). Gradient-echo EPI sequences were acquired with the following parameters: TR = 2000 ms, TE = 30 ms, flip angle = 77° , FOV = 220 mm, 32 slices, slice thickness = 4 mm, and matrix size = 64×63 (reconstructed to 64×64). Two dummy scans were acquired before rs-fMRI to allow for signal equilibrium. The total acquisition time was 3 minutes and 28 seconds, yielding 100 volumes. As regards t-fMRI acquisition, 66 participants (21 MDD, 45 BD) performed the same implicit emotion recognition task as in the UKB protocol, this time consisting of 4 blocks for each experimental condition (i.e., shapes and faces). Images were acquired using gradient-echo EPI sequences with TR = 3000 ms, TE = 35 ms, flip angle = 90° , FOV = 230 mm, and 40 axial slices with a thickness of 3 mm. The acquisition matrix was 80×80 , reconstructed to 128×128 . Two dummy scans were included at the start of each run to achieve signal stabilization. The total scan duration for t-fMRI was 6 minutes and 11 seconds, with 124 acquired volumes in total.

A separate sample of 223 patients (124 MDD, 99 BD) underwent MRI scanning on a Philips Ingenia CX (Philips, Netherlands) system equipped with a 32-channel SENSE head coil. Structural T1-weighted images were acquired using a 3D MPRAGE sequence with TR = 8.0 ms, TE = 3.7 ms, FOV = 256 mm, matrix = 256×256 , and an in-plane resolution of $1.0 \times 1.0 \text{ mm}^2$, yielding 182 axial slices at 1.0 mm thickness. DTI images were acquired for 183 patients (110 MDD, 73 BD) using a spin-echo echo-planar imaging (SE-EPI) sequence with the following parameters: TR = 5900 ms, TE = 78 ms, and FOV = 240 mm (anterior-posterior), 129 mm (foot-head), 232 mm (right-left). The acquisition included 56 contiguous axial slices, each 2.3 mm thick, reconstructed to an in-plane resolution of $1.88 \times 1.88 \text{ mm}^2$ (voxel size = $1.88 \times 1.88 \times 2.30 \text{ mm}^3$). Diffusion encoding was applied along 40 non-collinear directions using a b-value of 1000 s/mm^2 , with one additional b0 image. A SENSE acceleration factor of 2 was employed, and fat suppression was applied to minimize chemical shift artifacts. Resting-state fMRI scans were obtained

for 169 participants (95 MDD, 74 BD) using a gradient-echo EPI sequence (TR = 2000 ms, TE = 30 ms, flip angle = 85°, FOV = 192 mm). Thirty-eight interleaved ascending axial slices were acquired with 3.7 mm thickness and a 64×62 matrix, reconstructed to 96×96 pixels. Six dummy scans were performed before acquisition to reach longitudinal magnetization equilibrium. The total number of acquired volumes was 200, with an acquisition duration of 6 minutes and 56 seconds. Finally, t-fMRI data were acquired for 108 participants (61 MDD, 47 BD). Using gradient-echo EPI sequences, 192 functional volumes were acquired with TR = 2000 ms, TE = 30 ms, flip angle = 85°, and 38 axial slices with 3.7 mm of thickness. The acquisition matrix was 62×62 and reconstructed to 96×96 . To ensure signal stabilization, 5 dummy scans were performed before each run. The total duration of the t-fMRI acquisition was 6 minutes and 24 seconds.

3.2.2 T1-weighted imaging

The raw T1-weighted structural images were pre-processed with several FSL tools (Jenkinson et al., 2012), including BET (i.e., Brain Extraction Tool) (Smith, 2002), FLIRT (i.e., FMRIB's Linear Image Registration Tool) (Jenkinson et al., 2002; Jenkinson & Smith, 2001), FNIRT (i.e., FMRIB's Nonlinear Image Registration Tool) (Andersson et al., 2007a, b), and FAST (i.e., FMRIB's Automated Segmentation Tool) (Zhang et al., 2001). Specifically, after the full FOV raw T1-weighted images were defaced, the FOV was cut down, and a gradient distortion correction (GDC) was applied. To do so, BET and FLIRT were used, in conjunction with the MNI152 “nonlinear 6th generation” standard-space T1 template. T1 head images were then nonlinearly warped to MNI152 space using FNIRT. Finally, tissue-type segmentation was performed using FAST. The same images were also processed with FreeSurfer (Dale et al., 1999) version 6.0, through the *recon-all* command. This allowed the obtaining of 186 IDPs, including mean cortical thickness, surface area, and cortical volumes estimated for 62 ROIs according to the Desikan-Killiany-Tourville atlas (Desikan et al., 2006). Subcortical IDPs were further obtained using FIRST (FMRIB's Integrated Registration and Segmentation Tool) (Patenaude et al., 2011), which allowed for the estimation of 14 subcortical volumes.

3.2.3 Diffusion tensor imaging

Diffusion-weighted raw images were first corrected for eddy currents, head motion, and outlier slices using the Eddy tool (Andersson & Sotiropoulos, 2015, 2016). The corrected images were then fed into the DTI fitting tool (DTIFIT) to estimate several diffusion maps, including FA, AD, and RD, which were the diffusion indices considered in the current study. The DTI FA images were aligned onto a standard-space white matter skeleton using Tract-Based Spatial Statistics (TBSS) (Smith et al., 2006), which aligns the FA image onto a standard-space white-matter skeleton, along with a high-dimensional FNIRT-based warping to improve alignment (de Groot et al., 2013). The resulting standard-space warp was applied to all other DTI outputs. Finally, all DTI extracted measures were computed by averaging the skeletonized images of each map within a set of 48 standard-space tract masks defined by the Johns Hopkins University (JHU) White Matter Atlas (Mori et al., 2005; Wakana et al., 2007).

3.2.4 Resting-state fMRI

Resting-state MRI images were pre-processed by applying motion correction with MCFLIRT (Jenkinson et al., 2002), grand-mean intensity normalization by a single multiplicative factor, high-pass temporal filtering ($\sigma=50.0s$), EPI unwarping, and GDC unwarping. Structured artefacts were removed by ICA+FIX processing, that is, an independent component analysis followed by FMRIB's ICA-based X-noiseifier (Beckmann & Smith, 2004; Griffanti et al., 2014; Salimi-Khorshidi et al., 2014). The EPI unwarping consisted of a combined step including alignment to the T1 carried out by FLIRT, with a final boundary-based registration (BBR) cost function (Greve & Fischl, 2009). After GDC unwarping, a final FLIRT realignment to T1 was performed. For group-level network modelling, a group-average analysis was first built from 4,100 datasets. Each subject timeseries was temporally demeaned and variance-normalized (Beckmann & Smith, 2004). MELODIC's Incremental Group-PCA (MIGP) generated a group-PCA output, which served as input to group spatial-ICA in FSL's MELODIC tool (Beckmann & Smith, 2004; Hyvärinen, 1999). Spatial-ICA was applied at two different dimensionalities, i.e., $D=25$ and $D=100$, determining two different numbers of ICA components. Subject-specific node timeseries were obtained via the first stage of dual

regression (Filippini et al., 2009). For each subject, the D node-timeseries underwent network modelling, discarding the artefactual nodes, leaving D' nodes, and thus resulting in $D' \times D'$ matrices of connectivity estimates. Specifically, from the 25-dimensional group-ICA, 21 independent components (ICs) were kept as non-artefactual, while 55 ICs were kept from the 100-dimensional group-ICA. Network modelling was performed with the FSLNets toolbox (<http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/FSLNets>), estimating both full correlations and L_2 -regularized partial correlations (setting $\rho=0.5$) between node timeseries. Connectivity values were finally Gaussianized from Pearson r -values to z -values, with empirical correction for temporal autocorrelation. In the analyses reported here, we focused on the high-resolution 100-dimensional parcellation (i.e., the one resulting in 55 retained ICs), deriving 55×55 partial-correlation matrices per subject, which were then used to calculate the mean positive (Spos) and negative (Sneg) strength of functional connections for each IC using the Brain Connectivity Toolbox (<https://github.com/aestrivex/bctpy>). According to Jiang et al. (2023a), these 55 ICs can be grouped in nine resting-state networks, as reported in **Table 1**.

Table 1. Resting-state networks associated with the 55 non-artefactual ICs identified in UKB

Resting-state networks	IC enumeration
VAN	2, 15, 37, 45, 47
VIS	1, 3, 16, 8, 14
DMNp	5, 10, 11, 19, 36
SMN	6, 20, 22, 30, 32, 35
DMNa	7, 13, 21, 28, 52, 55
Sub&Cereb	38, 17, 23, 53, 54
DAN	4, 18, 27, 34, 39, 40, 41, 42
TempPar	9, 33, 43, 48, 50, 51
FPN	12, 24, 25, 26, 29, 31, 44, 46, 49

Abbreviations: IC, independent component; DMNa, anterior default mode network; DMNp, posterior default mode network; SMN, somatomotor network; Sub&Cereb, subcortical and cerebellar network; TempPar, temporoparietal network; VAN, ventral attention network; DAN, dorsal attention network; VIS, visual network; FPN, frontoparietal network.

3.2.5 Task-based fMRI

Task-based functional images were pre-processed similarly to the resting-state ones, except for spatial smoothing being applied before the intensity normalization, and for no artefact removal being carried out. Task-induced activation was modeled using FEAT (i.e., FMRIB's Expert Analysis Tool), and time-series statistical analysis was performed through FILM with local autocorrelation correction (Woolrich et al., 2001). Three activation contrasts between blocks were considered, namely Shapes, Faces, and Faces-Shapes. For each contrast, group-average activation maps (thresholded at $Z > 120$) were extracted across all subjects and used to generate 4 IDPs: the group-level fixed-effect z-statistic for Shapes, Faces, and Faces-Shapes, and the group-level fixed-effect z-statistic masked for the amygdala in the Faces-Shapes contrast. The Featquery tool was finally used to extract two different summary statistics, namely the median across voxels and the 90th percentile across voxels.

5.2.5.1 Habituation analyses

In addition to the mean activations for the above-mentioned contrasts, amygdala habituation measures were also extracted for both faces and shapes conditions. Of note, these parameters were extracted for all participants in the OSR cohort, and only in the subsample of 279 currently depressed individuals from the UKB. Indeed, amygdala habituation, defined as a response decrease over time due to repeated stimuli, has been suggested as a reliable fMRI phenotype reflecting emotion regulation (Plichta et al., 2014), and has been previously shown as disrupted in mood disorders and specifically associated with suicide attempts (Vai et al., 2023). First, mean activations for each block (i.e., 10 blocks in the UKB dataset and 8 blocks in the OSR sample) were modeled for each subject by performing a general linear model (GLM) using FEAT, setting the high-pass filter to 1/262 Hz, as it was previously suggested as the optimal threshold to attenuate linear scanner drifts and to capture habituation (Plichta et al., 2014). Then, the Featquery tool was used to extract the % change in blood oxygenation level dependent (BOLD) signal (i.e., the % signal change relative to the overall-image mean baseline level) for each block and participant within the amygdala ROI, which was selected from the Harvard-Oxford Subcortical Structural atlas (Caviness et al., 1996).

After extracting mean amygdala activation for each block, a regression approach was implemented in R (version 4.3.2) to quantify amygdala habituation, according to the methodology suggested by Plichta et al. (2014). Specifically, this approach considers all blocks in the calculation and involves the following regression equation:

$$y = bX + a$$

where the dependent variable y (i.e., % BOLD signal) is regressed on the log-transformed block order X to estimate habituation rate (i.e., coefficient b) and initial neural reactivity (i.e., intercept a). Since Montagu (1963) illustrated that the coefficient b is influenced by the intercept a , the absolute habituation index b' , which is not related to the initial response amplitude, can be computed using the following equation:

$$b' = b - c(a - \bar{a})$$

where the coefficient c represents the slope of b on a , and $\bar{a}$ denotes the average of the intercepts across the entire sample (Montagu, 1963). Based on these computations, negative values of b' indicate habituation, whereas positive b' values may suggest sensitization.

3.3 Genetic data

3.3.1 Genotyping, quality control, and imputation

All UKB participants underwent genome-wide genotyping performed with two highly overlapping arrays (i.e., the UK BiLEVE and the UK Biobank Axiom arrays) covering ~800,000 markers. A centralized QC was carried out on autosomal genotype data to account for possible array effects, batch effects, and plate effects (Bycroft et al., 2018). SNPs were additionally excluded based on missingness (i.e., >0.02) and Hardy-Weinberg equilibrium (i.e., $p < 10^{-8}$). Individuals were removed if they exhibited high levels of missing rates (i.e., >0.05), abnormal heterozygosity, relatedness of up to third-degree (i.e., KING $r < 0.044$) (Manichaikul et al., 2010), or phenotypic/genotypic sex discrepancy. Population structure within the UKB cohort was evaluated through PCA, and European ancestry was defined by 4-means clustering on the first two genetic principal components (Warren et al., 2017). A two-stage imputation was performed using the Haplotype Reference Consortium (HRC) and UK10K as reference panels (Bycroft et

al., 2018; McCarthy et al., 2016; Walter et al., 2015). Finally, poor imputed variants (i.e., $\text{INFO} \leq 0.4$) were excluded (McCarthy et al., 2016).

Among OSR participants, 320 (119 MDD, 201 BD) were genotyped through the Infinium PsychArray 24 BeadChip (Illumina, Inc., San Diego), which is a cost-effective, high-density microarray specifically developed in collaboration with the PGC for large-scale genetic studies focused on psychiatric predisposition and risk, covering almost 600,000 genetic variants, including ~50,000 markers previously associated with common psychiatric disorders, such as SCZ, BD, autism-spectrum disorders, ADHD, MDD, OCD, anorexia nervosa, and Tourette's syndrome (Illumina, 2025a). Moreover, 79 participants (51 MDD, 28 BD) were genotyped through the Infinium Global Screening Array-24 Kit (Illumina, Inc., San Diego) (Illumina, 2025b), combined with the Psych Booster. This kit includes 654,027 fixed markers along with an additional 30,000 markers from the Infinium PsychArray-24 BeadChip (Illumina, 2025c). Genotyped data underwent QC procedures, comparable to those conducted in the UKB, using PLINK 1.9 software (Purcell & Chang, 2007). Specifically, variants were excluded when having a low call rate (i.e., <0.02), a minor allele frequency $<1\%$, and a high deviance from Hardy-Weinberg equilibrium (i.e., $p < 10^{-8}$). Additionally, individuals were removed in case of phenotypic/genotypic sex mismatch, low genotype rate (i.e., <0.05), outlying autosomal heterozygosity (i.e., $F_{\text{het}} > \pm 0.2$), a close degree of relatedness with other individuals (i.e., identity by descent, $\text{IBD} > 0.1875$, halfway between second- and third- degree of relatedness), and a high deviance from the European population structure (i.e., >5 standard deviations from the mean of the first two genetic principal components). Genotype imputation was computed via the Michigan Imputation Server using Minimac4 (Das et al., 2016), selecting the latest version of the Haplotype Reference Consortium panel (i.e., HRC r1.1 2016) as reference panel, and setting the *rsq* filter to 0.3. This procedure allowed for the estimation of more than 10 million variants for each individual.

3.3.2 Polygenic scores estimation

PGSs for several psychiatric disorders, related medical conditions of interest, and inflammatory markers were computed as the sum of the number of effect alleles at each SNP position, weighted for their effect size derived from the latest and largest GWAS meta-analysis available at the time of conducting the analyses (see **Table 2** for detailed

information). Importantly, only GWASs for which summary statistics excluding the UKB sample were available were selected, to avoid bias or inflation in the estimation of PGSs within the current UKB cohort. Specifically, PGSs for each individual were calculated with the *-score* function of PLINK 1.9 as follows:

$$PRS_j = \sum_i^N \beta_i * dosage_{ij}$$

where j is the individual; N is the number of variants considered for the score of the disorder of interest; i is the genetic variant; *dosage* consists in the allele counts of variants associated with the disorder of interest; β is the weight reflecting the magnitude of association between variant alleles and the disorder derived from the reference GWAS. As far as β weights are concerned, they were estimated with LDpred2-auto. This is an R-based tool that allows for estimating the posterior mean causal effect sizes of each GWAS-included variant solely relying on the original GWAS summary statistics and an external Linkage Disequilibrium (LD) reference panel (Privé et al., 2021). Moreover, all GWAS-included variants underwent a QC procedure, excluding those markers whose standard deviation exceeded the one derived from the reference panel (Privé et al., 2022). Finally, before being used for subsequent analyses, PGSs were standardized within each cohort to a mean of 0 and a standard deviation of 1.

Table 2. Main information of GWAS studies that were used as a reference for calculating the adjusted weights of variants associated with the conditions of interest.

Traits of interest	Authors (year)	N. cases	N. controls	Ethnicity	PMID
MDD	MDD PGC (2025)	688,808	4,364,225	European	39814019
BD	O'Connell et al. (2025)	158,036	2,796,499	European	39843750
SCZ	Trubetskoy et al. (2022)	76,755	243,649	European	35396580
ADHD	Demontis et al. (2023)	38,691	186,843	European	36702997
Anorexia nervosa	Watson et al. (2019)	16,992	55,525	European	31308545
Autism	Grove et al. (2019)	18,381	27,969	European	30804558

Alcohol dependence	Walters et al. (2018)	14,904	37,944	Mixed	30482948
CUD	Johnson et al. (2020)	20,916	363,116	European	33096046
Generalized anxiety disorder	Kurki et al. (2023)	7,148	444,414	European	36653562
Neuroticism	de Moor et al. (2015)	63,661		European	25993607
OCD	IOCDF-GC and OCGAS (2018)	2,688	7,037	European	28761083
PTSD	Nievergelt et al. (2024)	137,136	1,085,746	European	38637617
Education	Lee et al. (2018)	766,345		European	30038396
BMI	Locke et al. (2015)	322,154		European	25673413
Coronary artery disease	Nikpay et al. (2015)	60,801	123,504	Mixed	26343387
C-reactive protein	Ligthart et al. (2018)	204,402		European	30388399
T2D	Verma et al. (2024)	154,194	278,454	European	39024449
Glycated hemoglobin	Willems et al. (2023)	122,446		European	39280063
LDL cholesterol, HDL cholesterol, Triglycerides	Graham et al. (2021)	1,654,960		Mixed	34887591
bNGF, CCL11, CCL2, CCL3, CCL4, CCL7, CSF1, CSF3, CTACK, CXCL1, CXCL10, CXCL12, CXCL9, FGFb, HGF, IFNg, IL1RA, IL1b, IL10, IL13, IL16, IL17, IL18, IL2, IL2RA, IL4, IL5, IL6, IL7, IL8, IL9, MIF, PDGFbb, RANTES, SCF, SCGFb, TNFa, TNFb, TRAIL, VEGF	Konieczny et al. (2025)	74,783		European	39794498

Abbreviations: ADHD, attention and hyperactivity disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CCL, C-C motif ligand; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; FGFb, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PTSD, post-traumatic stress disorder; RANTES, regulated on activation, normal T-cell expressed and secreted; SCF, stem cell factor; SCGFb,

stem cell growth factor beta; SCZ, schizophrenia; T2D, type 2 diabetes; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor.

3.4 Stress-related data

Stress-related variables included in the clustering analyses encompassed data on ACEs and stressful events encountered during adulthood. As previously mentioned, participants from the UKB cohort completed a comprehensive series of online questionnaires. Among these, ten items assessed stressful experiences during both childhood and adulthood, with responses rated on a 5-point Likert scale ranging from 0=“never true” to 4=“very often true”. Childhood stress was evaluated using five questions (Field IDs: 20487–20491) that assessed how well-loved, cared for, or abused participants were during childhood. These items were adapted from the Childhood Trauma Screener (CTS-5) (Glaesmer et al., 2013), a brief version of the widely used Childhood Trauma Questionnaire (CTQ), which measures the occurrence of adverse experiences in early life (Bernstein et al., 1998). Similarly, adulthood stress was assessed through five additional items (Field IDs: 20521–20525) that explored experiences of potentially abusive relationships in adult life. Individual item responses were coded and subsequently reverse-scored, such that a response of 4 indicated a higher degree of stress exposure (McManus et al., 2022). Total scores for both childhood and adulthood stress were calculated as the sum of the corresponding five items, yielding scores ranging from 0 to 20. However, given the collinearity between single items and the total scores, the latter were not included as input features of the clustering analyses to avoid the inclusion of redundant information.

In the OSR cohort, analogous measures were employed. Specifically, ACEs were assessed using the short form of the Childhood Trauma Questionnaire (CTQ-SF) (Bernstein et al., 2003), which includes 28 items covering the same five domains as the CTS-5: physical abuse, emotional abuse, physical neglect, emotional neglect, and sexual abuse. Each item is rated on a 5-point scale, yet only the total ratings for each specific domain were included in the analyses. Finally, to evaluate adulthood stress in the OSR cohort, the Schedule of Recent Experiences (SRE) (Holmes & Rahe, 1967) was administered. This instrument consists of a 43-item checklist capturing major and minor life events experienced over the previous three years. It enables the calculation of both

the total number of stressful events and a weighted score reflecting the relative intensity of stress or social adjustment required for each event.

3.5 Outcome variables assessment

To assess the clinical meaningfulness of the identified clusters, subtypes of depression were characterized in terms of several clinical profiles. First, depressive symptomatology was evaluated through the PHQ-9 and RDS-4 among UKB participants, and with the 13-item version of the BDI (Beck & Beck, 1972) and the 21-item version of the HAM-D scale (Hamilton, 1960) in the OSR cohort. While the BDI is a self-report questionnaire, the HAM-D scale was administered by patients' psychiatrists in charge. Given the relevance of comorbid medical conditions contributing to the heightened risk of mortality in depression, the presence of diabetes (Field ID: 2443) and cardiovascular diseases (including heart attacks, angina, stroke, and hypertension; Field ID: 6150) and BMI (Field ID: 21001) were evaluated in both cohorts. Treatment resistance was another outcome of interest considered in this study. In the UKB dataset, TRD cases were identified according to previously defined criteria by Fabbri et al. (2021), retrieving information on antidepressant treatments from primary care data. Specifically, to be considered as having TRD, individuals with lifetime MDD had to have experienced at least two switches between different antidepressant medications, regardless of drug class (a full list of antidepressant drugs can be found in the **Appendix Table A2**). Each antidepressant had to be prescribed for a minimum of six consecutive weeks, to ensure an adequate trial before switching and to reduce the likelihood that changes were due to adverse effects. Additionally, the time interval between the prescriptions of two consecutive antidepressants had to be no longer than 14 weeks, to confirm treatment continuity and exclude extended periods without pharmacological intervention (Fabbri et al., 2021). Conversely, among OSR patients, lifetime treatment resistance was defined according to the criteria proposed by Thase & Rush (1997) as a lack of response to a minimum of two antidepressant medications administered at therapeutically adequate doses and for appropriate durations. Indeed, despite some limitations of this operational definition (McAllister-Williams et al., 2020; Rush et al., 2019), it remains the most widely adopted standard in clinical settings to identify individuals suitable for TRD interventions (Brown et al., 2019a; Sforzini et al., 2022). Finally, suicidality was also one of the main

clinical outcomes of the study, considering either death thoughts (Field ID: 20437), self-harming behaviors (Field ID: 20480), and suicide attempts (Field ID: 20483). All the information regarding medical comorbidities, treatment resistance, and suicidality relative to OSR patients was assessed by their psychiatrists in charge, either through structured clinical interviews, medical charts, or information obtained from relatives. Death thoughts, in particular, were assessed by item 3 of the HAM-D scale and by item 8 of the BDI questionnaire.

In addition to clinical features, cognitive performance was also examined as a key outcome in the present study. For the UKB dataset, variables capturing working memory (Field ID: 100029), verbal fluency (Field ID: 100077), motor speed (Field ID: 100032), processing speed (Field ID: 502), and executive function (Field ID: 503) were extracted. All measures were collected at recruitment via a touchscreen questionnaire. Working memory was assessed with a digit sequencing task, in which participants reordered increasingly longer number sequences in ascending order; the number of digits correctly recalled (Field ID: 4259) served as the performance index. Verbal fluency was evaluated with a phonemic fluency task, requiring participants to generate as many words as possible beginning with a given letter within one minute, with the total word count (Field IDs: 10612) used as the outcome measure. Motor speed was assessed through 12 rounds of the card game *Snap*, where participants pressed a button box as quickly as possible when two identical cards appeared; the mean reaction time for correct responses (Field ID: 20023) was taken as the index of motor speed. Processing speed was measured with a symbol coding task, in which participants completed symbol-to-number matches within 90 seconds; the number of correct matches (Field ID: 23324) was used as the performance measure. Finally, executive function was evaluated using the Tower of London task, where participants determined the minimum number of moves needed to replicate a target configuration of colored balls placed on pegs; the number of correctly solved puzzles (Field ID: 21004) was used as the domain score.

In the OSR cohort, cognitive functioning was assessed with the Italian adaptation of the Brief Assessment of Cognition in Schizophrenia (BACS), which evaluates six domains (i.e., verbal memory, working memory, motor coordination, processing speed, executive functioning, and verbal fluency) via paper-and-pencil tasks (Anselmetti et al., 2008; Keefe et al., 2004). Working memory, verbal fluency, processing speed, and

executive function were assessed with the same tasks and scoring methods used in the UKB. Motor speed, however, was measured using the token motor task, in which participants transferred scattered tokens into a container over 60 seconds; the total number of tokens correctly placed was taken as the performance index. In addition, verbal memory was examined with a list-learning task, requiring participants to recall as many words as possible from a previously presented list; the total number of items recalled across five trials was used as the measure of performance in this domain.

3.6 Statistical analyses

3.6.1 Data pre-processing and harmonization

Before their inclusion in subsequent clustering analyses, all data modalities underwent rigorous pre-processing and harmonization procedures to mitigate potential confounding effects.

A critical initial step involved addressing potential batch effects present in our multimodal dataset, such as those arising from different MRI scanners or distinct genotype arrays. Indeed, batch effects are technical artefacts that can be attributable to differences in acquisition methodologies, rather than biological information, thereby representing undesirable sources of variance that can affect the consistency and replicability of results. Despite the availability of advanced harmonization techniques, such as *ComBat*, which have been suggested to correct for the so-called “scanner effects” (Fortin et al., 2018), recent evidence highlighted that the application of these methods on neuroimaging data can lower the predictive accuracy of ML methods, possibly due to the inadvertently removal of biologically relevant variance from the data (Belov et al., 2024). Therefore, a more conventional “within-array normalization” approach was adopted to both genetic and neuroimaging data as an alternative strategy for harmonization, as already widely employed in the genetics field (Dedeurwaerder et al., 2014). This procedure consists of scaling the data to the mean of 0 and standard deviation of 1 separately for each batch (i.e., genotyping array and MRI scanner). Indeed, standardizing data within each batch allows for reducing technical variability between batches while preserving the inherent biological signal (Dedeurwaerder et al., 2014).

Following batch harmonization, all input features were corrected for the potential nuisance effects of relevant covariates through linear regression. In particular, all data (except for PGSs) were corrected for age, sex, and antidepressant medication. In UKB, antidepressant medication was defined as a dichotomous variable indicating whether participants had ever taken any antidepressant drug (0=“no” and 1=“yes”, among the ones listed in the **Appendix Table A2**). Conversely, in the OSR cohort, the pharmacological load was estimated as a composite rating, summing a score of 1 for low-dose and a score of 2 for high-dose medications based on their antidepressant effect, as proposed by Sackeim (2001). Additionally, structural GM-derived measures were corrected for the volumetric scaling factor (Field ID: 25000) of each participant. Finally, the first six genetic principal components were used to correct PGSs for population structure, as they were shown to be the most ancestry-informative in previous studies (Coleman et al., 2020; Fabbri et al., 2022).

After harmonization and covariate correction, all data were standardized to a mean of 0 and a standard deviation of 1 to ensure an equal contribution of each feature to the downstream analyses, as well as to facilitate the interpretability of results’ directions.

Finally, given the high dimensionality of the included data, supplemental clustering analyses were conducted on dimensionally reduced datasets to assess whether dimensionality reduction would enhance the identification of homogeneous clusters. Specifically, dimensionality reduction was performed through PCA independently on each pre-processed data modality (i.e., GM, DTI, rs-fMRI, t-fMRI, PGSs, and stress-related data). Since the data within each modality were on the same scale, PCA was conducted on the corrected yet not standardized features, as standardization may distort the data (Lever et al., 2017). The number of principal components retained for each modality was determined using the Kaiser criterion (eigenvalues > 1), which aims to select components that explain more variance than a single original variable (Kaiser, 1960).

All these pre-processing steps were conducted in R (version 4.3.2), with PCA being specifically carried out using the package *psych* (Revelle, 2025).

3.6.2 Unsupervised machine learning analyses

To obtain homogeneous clusters of patients, a consensus clustering approach (Monti et al., 2003) was employed. This unsupervised ML pipeline has been specifically designed to obtain stable clustering solutions, thereby allowing for the detection of an optimal solution of clusters while guaranteeing the robustness and generalizability of findings. This approach was independently applied to distinct sets of input features. First, models on single modalities were run, including GM, DTI, rs-fMRI, t-fMRI, PGSs, and stress-related data, to systematically compare how different sources of heterogeneity might shape the phenotypical presentation of depression. Then, a multimodal model including all modalities that uncovered significant solutions of clusters was implemented to assess whether the combination of multiple levels of pathophysiological mechanisms would enhance the identification and characterization of homogeneous clusters. A full list of included variables of each dataset is provided in **Appendix Table A1**. Finally, the pipeline was performed on four distinct samples: 3,887 individuals with lifetime MDD and 279 currently depressed individuals with lifetime MDD (dMDD) from the UKB dataset; 211 depressed patients with MDD and 475 depressed MDD ($n=211$) and BD ($n=264$) patients from the OSR cohort. Notably, while the number of participants included was constant for all modalities within the UKB, it changed depending on the data's missingness for patients in OSR (see Results section for detailed information). In particular, the multimodal model included only those individuals who had data availability for all input features, with individuals having missing data for at least one modality being removed case-wise.

To implement the consensus clustering approach, the Python package *pyckmeans* was exploited (<https://github.com/TankredO/pyckmeans>). In line with the methodology proposed by Monti et al. (2003), this pipeline implemented an unsupervised ensemble clustering approach that combined multiple K-means partitions (π), where each K-means model was trained on a randomly selected subset of the data and a random subset of features (i.e., the so-called "random subspace"). Specifically, 1,000 iterations (H) were performed, resampling 80% of the data at each iteration. The predicted cluster memberships from individual clustering runs were aggregated into a consensus (or co-association) matrix (M). For each iteration $h \in \{1, \dots, H\}$, a temporary connectivity matrix $M^{(h)}$ was first defined, where its entries $M^{(h)}(i, j)$ were 1 if samples i and j were

clustered together, and 0 otherwise. The final consensus matrix M , an $N \times N$ matrix where N is the total number of observations, was then computed as the normalized sum of the connectivity matrices over all H iterations. The formula for the consensus index $M(i, j)$ suggested by Monti et al. (2003) is the following:

$$M(i, j) = \frac{\sum_{h=1}^H M^{(h)}(i, j)}{\sum_{h=1}^H I^{(h)}(i, j)}$$

where $I^{(h)}(i, j)$ is an indicator matrix that is equal to 1 if both samples i and j are present in the h -th resampled dataset $D^{(h)}$, and 0 otherwise. The entry $M(i, j)$ thus recorded the frequency with which a pair of samples was clustered together, given that they both appeared in the resampled subset. This matrix, interpreted as a similarity matrix, was subsequently used to derive the final consensus clustering by applying a secondary hierarchical clustering step. Specifically, the matrix $1 - M$ was used as a new distance matrix for agglomerative hierarchical clustering to ensure that samples with the highest consensus index were placed adjacent to each other (Monti et al., 2003).

As represented in **Figure 5**, this procedure was iterated for multiple clustering solutions, ranging from 2 to 5 possible clusters. The optimal k was then determined based on the evaluation of two internal consistency metrics, the Davies-Bouldin Index and the Silhouette Score. Specifically, for each model, the optimal clustering solution was defined as the one yielding the highest Silhouette score and the lowest Davies-Bouldin index.

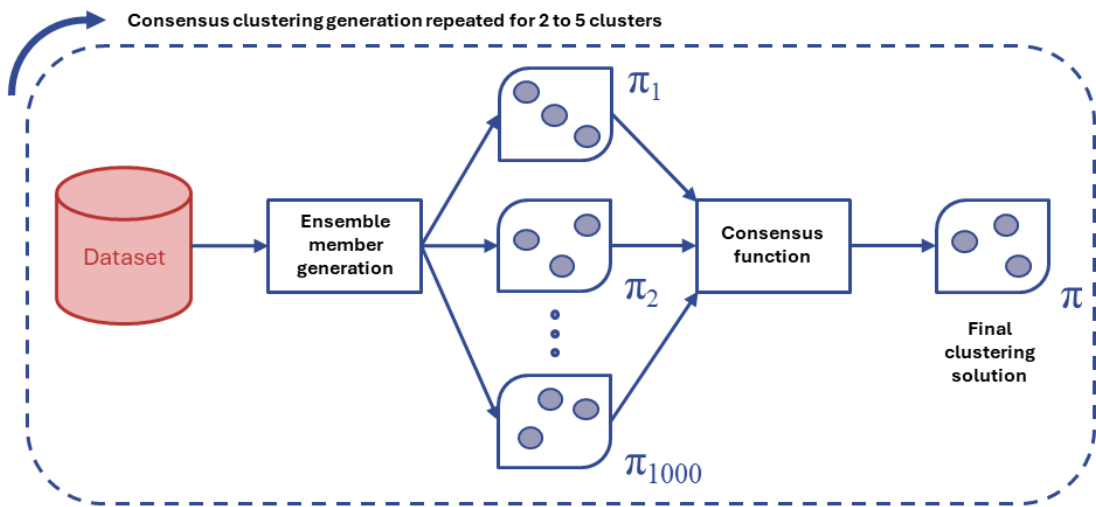


Figure 5. Graphical representation of the consensus clustering approach as implemented in the current study.

Finally, to assess the statistical validity of the optimal clustering solutions and determine whether they truly represented distinct subgroups rather than random variations within a homogeneous population, a Monte Carlo simulation-based approach was employed. Specifically, the *sigclust* method (Liu et al., 2008) was applied to each feature set, using 10,000 simulations to test the null hypothesis that the data were generated from a single multivariate Gaussian distribution. Only clustering solutions within the UKB dataset that met a significance threshold of False Discovery Rate (FDR) corrected *p-value* (i.e., *q-value*) < 0.05 were considered to reflect statistically meaningful data-driven subtypes, and were thereby replicated among the OSR cohort.

Remarkably, while analyses for OSR samples were conducted on local computers, analyses for UKB datasets were run within the Research Analysis Platform (RAP), a cloud-based environment that enables running analyses through several built-in tools and several programming languages via JupyterLab (UK Biobank, 2025).

3.6.3 Clusters' characterization

To evaluate the clinical and biological relevance of the identified clustering solutions, each significant partition was compared across all input and outcome features using statistical tests appropriate to the measurement scale and their data distribution. While the number of individuals to be compared for input features was the same included in each stratification model, the sample size of subjects varied across outcomes' comparisons, as missing data were removed case-wise. Continuous variables were first tested for normality using the Shapiro–Wilk test and for homogeneity of variance using Levene's test (both at $\alpha = 0.05$). When assumptions of normality and equal variance were met, comparisons between two clusters were conducted using Student's t-tests with pooled variance, whereas the Wilcoxon rank-sum test was applied otherwise. For solutions with more than two clusters, one-way ANOVA or Kruskal–Wallis tests were used under the same criteria. Effect sizes for continuous variables were quantified using Hedges' *g* for two-group comparisons and η^2 or ε^2 for ANOVA and Kruskal–Wallis tests, respectively. Dichotomous variables were compared using Pearson's χ^2 tests, or Fisher's exact tests when expected cell counts were below five. For larger contingency tables, Cramer's *V* was reported as a measure of association strength, and odds ratios were computed for pairwise contrasts. Ordinal categorical variables were analyzed using the

Wilcoxon rank-sum test for two clusters, with the point-biserial correlation coefficient as an effect size, or the Kruskal–Wallis test for more than two clusters, with ε^2 as a measure of effect magnitude. All *p-values* were corrected for multiple testing using the FDR thresholding (Benjamini & Hochberg, 2000) as implemented in R (version 4.3.2) through the *p.adjust* function. All analyses were conducted in R (version 4.3.2) using the *dplyr* (Wickham, 2015), *rstatix* (Kassambara, 2023), *effsize* (Torchiano, 2020), *car* (Fox & Weisberg, 2018), and *FSA* (Ogle et al., 2025) packages.

3.6.4 Supervised prediction of outcomes

To assess the translational value of the identified clusters, supervised ML models were trained with two complementary objectives. First, we used the same features that defined the significant clustering solutions to predict cluster membership. The performance of these models would serve as an external validation metric for the defined subtypes, as higher performances would be indicative of non-overlapping groups. Moreover, these models would provide insights regarding the possibility of assigning new subjects to the identified clusters, thanks to the cross-validation procedure (Varoquaux et al., 2018), thereby providing a possible tool to assess the individual risk of belonging to a specific depression subtype that may benefit from personalized treatment strategies. Secondly, we trained models separately within each cluster, again using the same features, to predict clinically relevant outcomes of interest, including treatment resistance, cardiometabolic disorders, and self-harming behaviors (i.e., the dichotomous outcome variables being shared by both UKB and OSR datasets, as described in section 3.5). By comparing the performance and the feature-outcome relationships across clusters, these models would allow us to assess whether risk associations might differ by subgroup.

Given the high collinearity of the input features used for the clustering analyses, an elastic net penalized regression was implemented through a 5-fold nested cross-validation. Indeed, the elastic net penalization consists of the combination of L_1 and L_2 regularizations, which allows for variable selection while also handling multicollinearity, by selecting or omitting groups of highly correlated predictors (Ogut et al., 2012; Pavlou et al., 2016). In line with this, the regression coefficients $\hat{\beta}$ are calculated as follows:

$$\hat{\beta} = \frac{\sum_{i=1}^N (Y_i - \sum_{j=1}^p \beta_j X_{ij})^2}{2n} + \lambda \left(\frac{(1 - \alpha)}{2} \sum_{j=1}^p \beta_j^2 + \alpha \sum_{j=1}^p |\beta_j| \right)$$

where Y_i is the independent variable for the i -th observation; X_{ij} is the value of the j -th predictor for the i -th observation; N is the number of observations; p is the number of predictors; λ is the tuning parameter that controls the strength of the penalization; α is the mixing parameter ranging from 0 to 1 that specifies the trade-off between L_1 (i.e., $\sum_{j=1}^p |\beta_j|$) and L_2 (i.e., $\sum_{j=1}^p \beta_j^2$) penalizations (Zou & Hastie, 2005). Both λ and α hyperparameters were optimized within the nested cross-validation scheme, selecting values that allowed for the highest predictive performance within the inner loop of cross-validation. Specifically, λ ranged over a set of 6 values (i.e., 0.01, 0.1, 1, 10, 100, 1000), whereas α was optimized within a set of 11 linearly spaced values ranging from 0 to 1 (i.e., 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8, 0.9, 1). Within the cross-validation scheme, a random subsampling procedure was additionally employed to avoid the putative inflation of classification accuracy in case of class imbalance, which can lead to the systematic prediction of the majority class.

To assess the significance of the predictive models, 1000 permutations significance tests were performed (Ojala & Garriga, 2010). In this procedure, the correspondence between predictors and class labels was disrupted by randomly permuting the outcome variable, thereby generating a null distribution of classification accuracies expected under random association. For each permutation, a classifier was trained on the shuffled data, and the resulting accuracies were aggregated to form this null distribution. The statistical significance of the original model's accuracy was then determined by computing the proportion of permuted models that achieved performance equal to or greater than the observed accuracy.

For models exhibiting performance significantly above chance level, feature importance was subsequently estimated to identify the predictors contributing most strongly to the classification. Specifically, a bootstrap resampling approach with 1000 iterations was employed across cross-validation folds to derive stable estimates of coefficient variability. Features were considered meaningful contributors when their bias-corrected bootstrapped confidence intervals did not include zero (i.e., at the 95% confidence level).

All the supervised ML analyses were conducted in Python using the *CVPCR* package, adapting the source code available at <https://github.com/fcalesella/CVPCR>.

4. Results

Descriptive statistics of the entire samples for both UKB (n. MDD = 3,887 and n. dMDD = 279) and OSR (n. MDD = 211 and n. BD = 264) are reported in **Table 3** and **Table 4**, respectively. Specifically, among the OSR sample, MDD patients showed significantly higher age ($q\text{-value}=0.020$), age of onset ($q\text{-value}=0.021$), current ($q\text{-value}=0.008$) and past ($q\text{-value}=0.002$) history of TRD compared to BD patients, while BD patients had significantly higher BMI ($q\text{-value}=0.004$), number of depressive episodes ($q\text{-value}<0.001$), death thoughts (HAM-D item 3, $q\text{-value}=0.004$; BDI item 8, $q\text{-value}=0.045$), and significantly lower performance in verbal fluency ($q\text{-value}=0.005$) compared to patients with MDD.

Table 3. Descriptive statistics of the UKB sample, including all individuals with lifetime MDD and the currently depressed ones (dMDD).

Variable	Field ID or definition	MDD (n=3,887)	dMDD (n=279)
Age	21003	57.97 ± 4.84	57.08 ± 4.90
Sex	31	0: 2665, 1: 1222	0: 187, 1: 92
BMI	21001	26.75 ± 4.74	28.08 ± 5.87
Number of depression episodes	4620	6.84 ± 33.36	19.70 ± 45.34
Antidepressant medication	See Appendix Table A2	0: 3327, 1: 560	0: 195, 1: 84
Ever attempted suicide	20483	0: 3668, 1: 203	0: 246, 1: 30
Ever self-harmed	20480	0: 3468, 1: 403	0: 219, 1: 57
Death thoughts	20437	0: 1366, 1: 2186	0: 64, 1: 193
RDS-4	Sum of 2050, 2060, 2070, 2080	6.03 ± 2.30	11.91 ± 1.94
PHQ-9	Sum of 20507, 20508, 20510, 20511, 20513, 20514, 20517, 20518, 20519	4.40 ± 4.70	11.48 ± 6.43
Cardiovascular diseases	6150	0: 3289, 1: 598	0: 218, 1: 61
Diabetes	2443	0: 3801, 1: 81	0: 265, 1: 13
TRD – history	Derived from Fabbri et al. (2021)	0: 1061, 1: 63	0: 88, 1: 19
Working memory	4259	5.91 ± 1.30	5.91 ± 1.45
Verbal fluency	10612	20.27 ± 7.76	23.00 ± NA
Motor speed	20023	571.17 ± 97.18	580.35 ± 107.84
Processing speed	23324	20.70 ± 4.84	20.49 ± 5.45
Executive function	21004	10.51 ± 3.13	10.19 ± 3.23

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; dMDD, depressed individuals with lifetime MDD; MDD, major depressive disorder; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms; TRD, treatment-resistant depression.

Table 4. Descriptive statistics of the OSR sample, comparing MDD and BD groups.

Variable	MDD (n=211)	BD (n=264)	Statistic	p-value	q-value	Direction
Age	50.41 ± 10.12	47.80 ± 10.69	23823.5	0.007	0.020*	MDD > BD
Sex	0: 138, 1: 73	0: 165, 1: 99	0.427	0.513	0.632	MDD > BD
BMI	24.96 ± 4.70	26.45 ± 4.94	29881.5	<0.001	0.004*	BD > MDD
Education	12.95 ± 3.97	12.17 ± 3.77	24961	0.049	0.095	MDD > BD
Age of onset	32.51 ± 11.91	29.47 ± 10.29	23797	0.008	0.021*	MDD > BD
Number of depressive episodes	5.38 ± 5.65	8.25 ± 7.99	33961.5	<0.001	<0.001*	BD > MDD
Pharmacological load	5.08 ± 2.59	4.86 ± 2.29	27023	0.686	0.758	MDD > BD
History of suicide attempts	0: 169, 1: 41	0: 207, 1: 52	0.022	0.881	0.921	MDD > BD
HAM-D – total score	22.09 ± 6.78	22.00 ± 5.60	25338.5	0.989	0.989	MDD > BD
HAM-D – item 3	0: 80, 1: 65, 2: 28, 3: 16, 4: 2	0: 103, 1: 116, 2: 19, 3: 7, 4: 0	/	<0.001	0.004*	BD > MDD
BDI – total score	16.45 ± 7.96	15.92 ± 8.30	13830.5	0.452	0.612	MDD > BD
BDI – item 8	0: 81, 1: 49, 2: 16, 3: 3	0: 119, 1: 44, 2: 10, 3: 11	9.875	0.019	0.045*	BD > MDD
Cardiovascular disorders	0: 160, 1: 51	0: 214, 1: 49	2.158	0.142	0.251	BD > MDD
Diabetes	0: 205, 1: 6	0: 246, 1: 18	3.861	0.049	0.095	BD > MDD
TRD – history	0: 146, 1: 59	0: 221, 1: 38	13.770	<0.001	0.002*	MDD > BD
TRD – current	0: 146, 1: 59	0: 215, 1: 44	9.213	0.002	0.008*	MDD > BD
BACS – verbal memory	35.86 ± 10.86	34.58 ± 10.78	-1.15	0.248	0.366	MDD > BD
BACS – working Memory	17.14 ± 5.85	16.80 ± 5.21	17360.5	0.522	0.632	MDD > BD
BACS – psychomotor coordination	65.39 ± 17.42	65.41 ± 21.64	15777	0.692	0.758	BD > MDD
BACS – verbal fluency	12.20 ± 4.83	10.79 ± 4.42	14857	0.001	0.005*	MDD > BD
BACS – processing speed	37.32 ± 13.73	35.57 ± 12.88	15674.5	0.254	0.366	MDD > BD
BACS – executive functions	14.07 ± 4.49	14.74 ± 4.06	12397.5	0.200	0.329	BD > MDD

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BACS, Brief Assessment of Cognition in Schizophrenia; BD, bipolar disorder; BDI-SF, Beck Depression Inventory; BMI, body mass index; HAM-D, Hamilton Depression Rating Scale; MDD, major depressive disorder; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Additional descriptive statistics were conducted to compare either the UKB MDD (Table 5) or the UKB dMDD (Table 6) samples to the OSR MDD sample for the overlapping demographic variables. According to these comparisons, both UKB cohorts had significantly older age ($q\text{-value}<0.001$), higher BMI ($q\text{-value}<0.001$) with respect to the MDD cohort from OSR (Table 5 and Table 6). On the other hand, the OSR MDD sample showed significantly higher rates of cardiovascular comorbidities ($q\text{-value}<0.001$), TRD ($q\text{-value}<0.001$), and history of suicide attempts ($q\text{-value}<0.001$) as

compared to the wider UKB MDD sample (**Table 5**), with the rate of individuals attempting suicide being increased in the OSR MDD sample also in comparison to the UKB dMDD sample ($q\text{-value}=0.019$; **Table 6**).

Table 5. Descriptive statistics of the overlapping demographic variables between the UKB MDD and the OSR MDD sample.

Variable	UKB MDD (n=3,887)	OSR MDD (n=211)	Statistic	p-value	q-value	Direction
Age	57.97 ± 4.84	50.41 ± 10.12	600207.5	<0.001	<0.001*	UKB > OSR
Sex	1: 1222, 0: 2665	1: 73, 0: 138	0.92	0.336	0.384	OSR > UKB
BMI	26.75 ± 4.74	24.96 ± 4.70	469288	<0.001	<0.001*	UKB > OSR
Number of depressive episodes	6.84 ± 33.36	5.38 ± 5.65	88773	<0.001	<0.001*	UKB > OSR
History of suicide attempts	0: 3668, 1: 203	0: 169, 1: 41	72.25	<0.001	<0.001*	OSR > UKB
Cardiovascular disorders	0: 3289, 1: 598	0: 160, 1: 51	11.59	<0.001	<0.001*	OSR > UKB
Diabetes	0: 3801, 1: 81	0: 205, 1: 6	/	0.456	0.456	OSR > UKB
TRD – history	0: 1061, 1: 63	0: 146, 1: 59	111.70	<0.001	<0.001*	OSR > UKB

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; MDD, major depressive disorder; OSR; IRCCS Ospedale San Raffaele; TRD, treatment-resistant depression; UKB, UK Biobank. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Table 6. Descriptive statistics of the overlapping demographic variables between the UKB dMDD and the OSR MDD sample.

Variable	UKB dMDD (n=279)	OSR MDD (n=211)	Statistic	p-value	q-value	Direction
Age	57.08 ± 4.90	50.41 ± 10.12	41006.5	<0.001	<0.001*	UKB > OSR
Sex	1: 92, 0: 187	1: 73, 0: 138	0.14	0.707	0.707	OSR > UKB
BMI	28.08 ± 5.87	24.96 ± 4.70	36605	<0.001	<0.001*	UKB > OSR
Number of depressive episodes	19.70 ± 45.34	5.38 ± 5.65	8402	0.052	0.083	UKB > OSR
History of suicide attempts	0: 246, 1: 30	0: 169, 1: 41	7.16	0.007	0.019	OSR > UKB
Cardiovascular disorders	0: 218, 1: 61	0: 160, 1: 51	0.36	0.547	0.625	OSR > UKB
Diabetes	0: 265, 1: 13	0: 205, 1: 6	1.08	0.299	0.399	UKB > OSR
TRD – history	0: 88, 1: 19	0: 146, 1: 59	4.56	0.033	0.066	OSR > UKB

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; dMDD, depressed individuals with lifetime MDD; MDD, major depressive disorder; OSR; IRCCS Ospedale San Raffaele; TRD, treatment-resistant depression; UKB, UK Biobank. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

4.1 Main analyses on UKB samples

4.1.1 Unsupervised stratification models

The consensus clustering approach on single modalities led to the identification of 2 homogeneous clusters for both MDD (**Table 7**) and dMDD (**Table 8**) samples of the UKB, except for the stratification model on rs-fMRI on the whole MDD sample, which uncovered a solution of 4 clusters. All clustering solutions were statistically significant ($q\text{-value} < 0.05$), except for the two stratification models conducted on stress-related data, whose solutions were not significant (see **Table 7** and **Table 8**). Therefore, the multimodal model included data for GM, DTI, rs-fMRI, t-fMRI, and PGSs. This allowed for a significant clustering solution of 2 clusters with a $q\text{-value} < 0.001$ and a $q\text{-value} = 0.002$ in the MDD and dMDD samples, respectively.

Among the stratification models conducted on the dimensionally-reduced features, most of the clustering solutions were not statistically significant. Only the clustering conducted on t-fMRI data yielded a 3- and a 5-cluster solution in the MDD and dMDD samples, respectively, while the stress-based stratification model uncovered a significant 4-cluster solution in both MDD and dMDD samples (see **Appendix Table A3** and **Appendix Table A4**, respectively, for detailed statistics).

Table 7. Summary of consensus clustering models among the MDD sample of UKB.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	Cl0: 1845, Cl1: 2042	0.08	3.15	<0.001*
DTI	2	Cl0: 1711, Cl1: 2176	0.14	2.21	<0.001*
rs-fMRI	4	Cl0: 766, Cl1: 1257, Cl2: 1021, Cl3: 843	0.03	4.03	<0.001*
t-fMRI	2	Cl0: 1514, Cl1: 2373	0.30	1.20	<0.001*
PGSs	2	Cl0: 1945, Cl1: 1942	0.07	3.30	<0.001*
Stress	2	Cl0: 464, Cl1: 3423	0.41	1.71	1
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	2	Cl0: 2030, Cl1: 1857	0.05	4.41	<0.001*

Abbreviations: Cl, cluster; GM, grey matter; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI.

*Statistical significance at FDR-corrected p-value (i.e., q-value) < 0.05

Table 8. Summary of consensus clustering models among the dMDD sample of UKB.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	C10: 136, C11: 143	0.08	3.10	<0.001*
DTI	2	C10: 125, C11: 154	0.14	2.18	<0.001*
rs-fMRI	2	C10: 122, C11: 157	0.06	3.92	0.004*
t-fMRI	2	C10: 90, C11: 189	0.27	1.46	<0.001*
PGSs	2	C10: 127, C11: 152	0.08	3.06	0.007*
Stress	2	C10: 43, C11: 236	0.36	1.57	0.301
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	2	C10: 130, C11: 149	0.05	4.04	0.002*

Abbreviations: *Cl*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *PGSs*, polygenic scores; *rs-fMRI*, resting-state fMRI; *Sil*, Silhouette score; *t-fMRI*, task-based fMRI. *Statistical significance at FDR-corrected *p*-value (i.e., *q*-value) <0.05

4.1.2 Clinical and neurobiological characterization of clusters

The identified significant clusters using the non-dimensionally reduced datasets were subsequently compared in terms of both input features utilized for the clustering analyses and the outcome variables of interest described in section 3.5. The following paragraphs will provide an overview of the significant comparisons for each stratification model among the MDD and dMDD samples of UKB. Full statistics of input feature comparisons, including the non-significant ones, can be found in **Appendix Table A5** for the MDD sample and in **Appendix Table A6** for the dMDD sample. Full statistics of outcome variables are reported in **Appendix Table A7** and **Appendix Table A8** for the MDD and dMDD samples, respectively.

4.1.2.1 Stratification models in the MDD sample of UKB

The stratification model conducted on GM yielded 2 different clusters. As represented in **Figure 6** and reported in **Appendix Table A5**, one cluster (C10, 47.46% of the sample) was characterized by a widespread pattern of increased surface area (*q*-value<0.001), reduced cortical and subcortical GM volumes (*q*-value<0.001), and lower cortical thickness (*q*-value<0.001) with respect to the other cluster (C11). In particular, the most pronounced effect sizes were observed on cortical thickness, especially in the

bilateral inferior parietal and superior frontal gyri, precuneus, precentral and supramarginal gyri (**Appendix Table A5**). Interestingly, the more neurobiologically compromised cluster (C10) was also characterized by a significantly higher rate of comorbid diabetes ($q\text{-value}<0.001$, **Table 9** and **Appendix Table A7**).

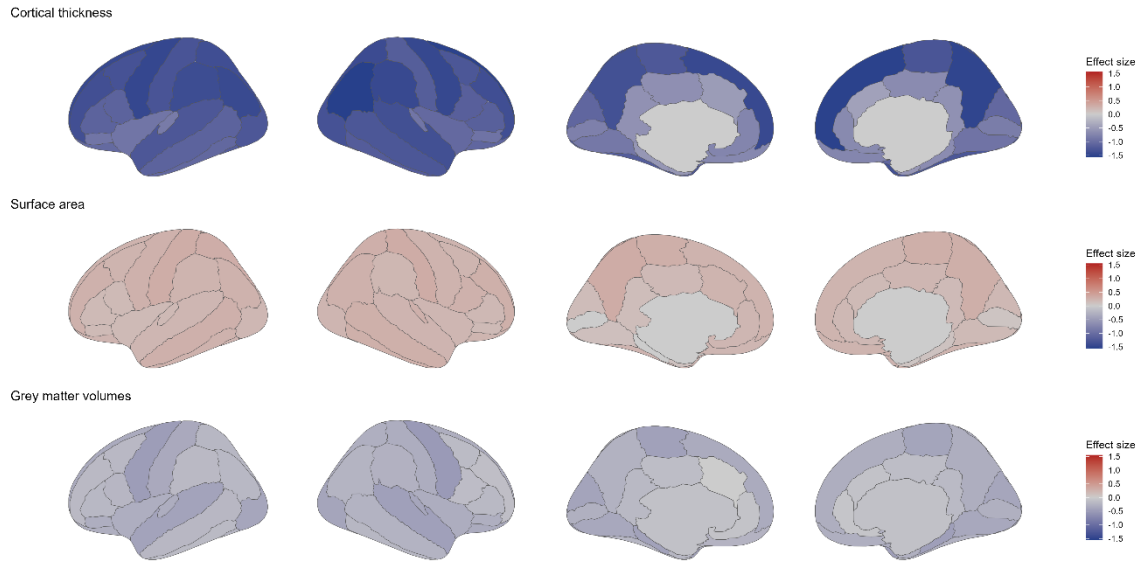


Figure 6. Effect sizes (Hedges' g) of significant input features comparing clusters from the GM-based stratification model among the MDD sample of the UKB dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

Table 9. Significant outcome variable comparisons between clusters resulting from the GM stratification model among the MDD sample of UKB.

Variable	C10	C11	Statistic	p-value	q-value
Diabetes	0=1784; 1=58	0=2017; 1=23	19.36	<0.001	<0.001*

Abbreviations: Cl, cluster. *Statistical significance at FDR-corrected $p\text{-value}$ (i.e., $q\text{-value}$) <0.05

In the 2-cluster solution obtained with DTI, one cluster (C10, 44.01%) showed decreased values of FA ($q\text{-value}<0.001$), along with higher values of both AD ($q\text{-value}<0.001$) and RD ($q\text{-value}<0.001$) in all white matter tracts (see **Figure 7** and **Appendix Table A5**). Specifically, FA and RD values within the bilateral anterior, posterior, and superior corona radiata, the corpus callosum, and the superior longitudinal fasciculi displayed the highest effect sizes (**Appendix Table A5**). The same cluster also

exhibited a higher rate of cardiovascular diseases ($q\text{-value}=0.007$), as well as slower motor ($q\text{-value}<0.001$) and processing ($q\text{-value}=0.006$) speed (**Table 10** and **Appendix Table A7**).

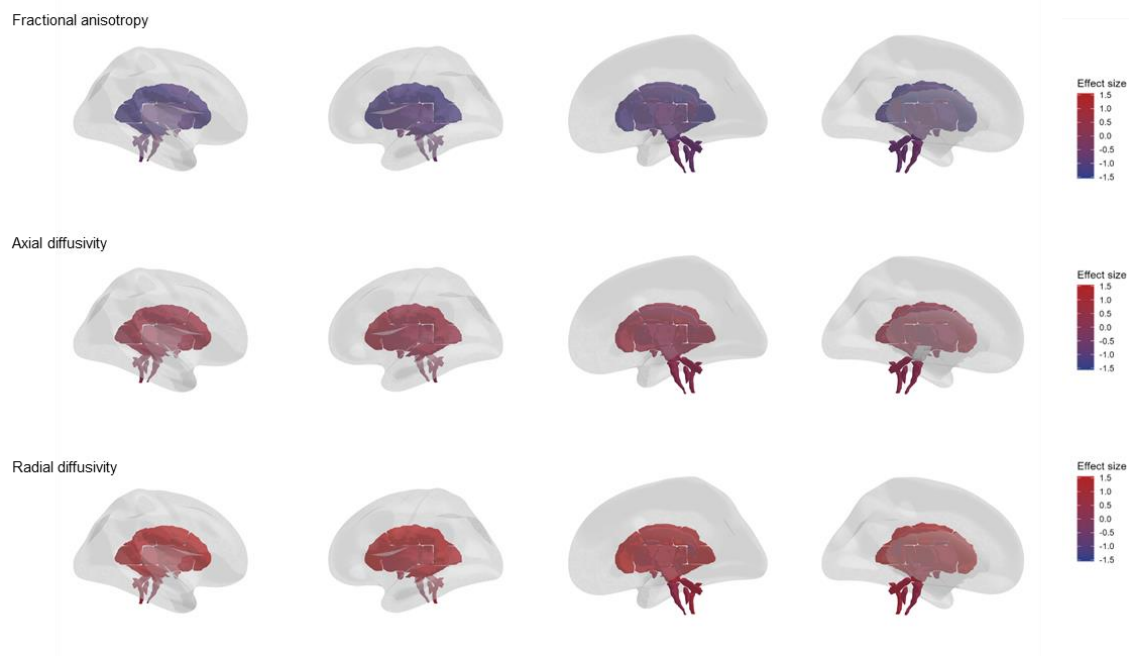


Figure 7. Effect sizes (Hedges' g) of significant input features comparing clusters from the DTI-based stratification model among the MDD sample of the UKB dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

Table 10. Significant outcome variable comparisons between clusters resulting from the DTI stratification model among the MDD sample of UKB.

Variable	C10	C11	Statistic	p-value	q-value
Cardiovascular diseases	0=1412; 1=299	0=1877; 1=299	10.26	0.001	0.007*
Diabetes	0=1663; 1=46	0=2138; 1=35	5.47	0.019	0.065
RDS-4	5.97 ± 2.31	6.07 ± 2.29	1628382	0.044	0.089
PHQ-9	4.29 ± 4.71	4.48 ± 4.69	1744552.5	0.042	0.089
TRD – history	0=487; 1=37	0=574; 1=26	3.93	0.047	0.089
BMI	26.59 ± 4.75	26.87 ± 4.73	1777219	0.022	0.065
Motor speed	578.54 ± 100.36	565.35 ± 94.21	1816535.5	<0.001	<0.001*
Processing speed	20.33 ± 4.83	20.97 ± 4.84	607133	0.001	0.006*

Abbreviations: BMI, body mass index; Cl, cluster; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected $p\text{-value}$ (i.e., $q\text{-value}$) <0.05

Regarding the rs-fMRI-based stratification model, 4 distinct clusters were identified. Among these clusters, C12 (26.26%) showed a widespread pattern of weaker negative strength of resting-state connections ($q\text{-value}<0.001$), while C10 (19.71%) had generally higher positive strength of resting-state connections ($q\text{-value}<0.001$), as visible in **Figure 8** and **Appendix Table A5**, with respect to the other three clusters. Effect sizes for both Spos and Sneg were most pronounced among the ICs enumerated as 1, 3, 4, 8, 14, and 16 (**Appendix Table A5**), all primarily belonging to the visual network (see correspondence in **Table 1**). These differences were further accompanied by a significant difference in BMI values (**Table 11** and **Appendix Table A7**).

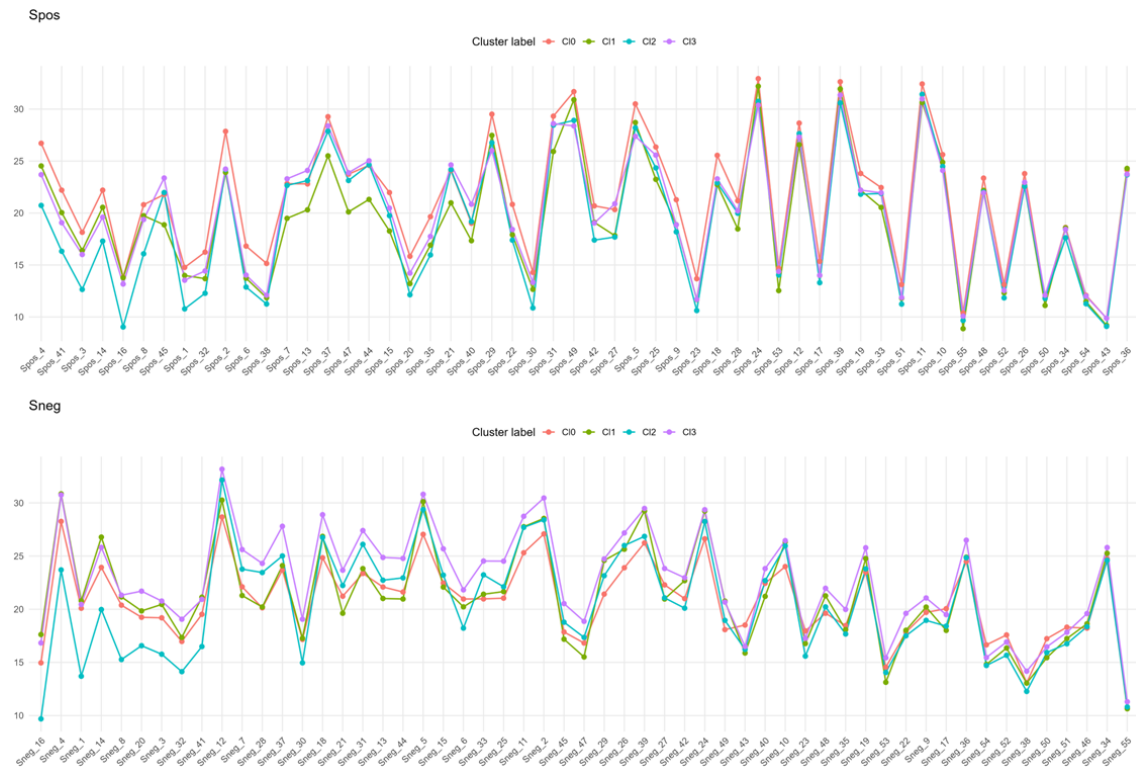


Figure 8. Mean scores of the significant strength of positive (Spos) and negative (Sneg) connections of resting-state networks comparing clusters from the rs-fMRI-based stratification model among the MDD sample of the UKB dataset. Networks are ordered based on effect size (Hedges' g).

Table 11. Significant outcome variable comparisons between clusters resulting from the rs-fMRI stratification model among the MDD sample of UKB.

Variable	C10	C11	C12	C13	Statistic	p-value	q-value
Cardiovascular diseases	0=653; 1=113	0=1044; 1=213	0=853; 1=168	0=739; 1=104	9.50	0.023	0.117

PHQ-9	4.55 ± 4.61	4.25 ± 4.65	4.71 ± 4.98	4.09 ± 4.48	11.07	0.011	0.085
BMI	27.90 ± 5.15	26.90 ± 4.76	26.71 ± 4.63	25.51 ± 4.13	112.05	<0.001	<0.001*

Abbreviations: BMI, body mass index; CI, cluster; PHQ-9, Patient Health Questionnaire-9. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

The data-driven stratification employing t-fMRI data identified 2 significant clusters, one of which (CI0, 38.95%) exhibited a decreased mean activation for both faces ($q\text{-value}<0.001$) and shapes ($q\text{-value}<0.001$) conditions (**Figure 9** and **Appendix Table A5**). In addition, the same cluster was characterized by a significantly higher current depressive symptomatology ($q\text{-value}=0.033$), a higher rate of cardiovascular diseases ($q\text{-value}=0.008$), higher BMI ($q\text{-value}<0.033$), and lower performance in processing speed ($q\text{-value}=0.004$). For detailed statistics, see **Table 12** and **Appendix Table A7**.

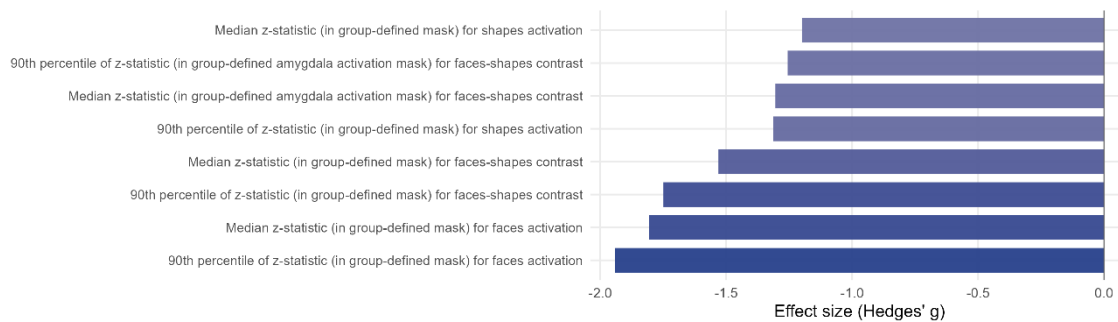


Figure 9. Effect sizes (Hedges' g) of significant input features comparing clusters from the t-fMRI-based stratification model among the MDD sample of the UKB dataset. All negative values (blue) indicate higher values in CI1 than in CI0.

Table 12. Significant outcome variable comparisons between clusters resulting from the t-fMRI stratification model among the MDD sample of UKB.

Variable	CI0	CI1	Statistic	p-value	q-value
Cardiovascular diseases	0=1245; 1=269	0=2044; 1=329	10.82	0.001	0.008*
RDS-4	6.13 ± 2.33	5.96 ± 2.28	1708680.5	0.008	0.033*
PHQ-9	4.64 ± 4.87	4.24 ± 4.58	1822728	0.024	0.071
BMI	27.00 ± 4.90	26.59 ± 4.63	1881471.5	0.009	0.033*
Processing speed	20.31 ± 4.81	20.97 ± 4.85	594829	<0.001	0.004*

Abbreviations: BMI, body mass index; CI, cluster; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Using PGSs alone, the consensus clustering approach uncovered a 2-cluster solution, with one cluster (C10, 50.03%) showing higher levels of PGSs for inflammatory markers ($q\text{-value}<0.001$), BMI ($q\text{-value}=0.022$), CRP ($q\text{-value}=0.009$), T2D ($q\text{-value}=0.024$), and lower values of the PGS for HDL cholesterol ($q\text{-value}=0.032$). **Appendix Table A5** provides the detailed statistics of the comparisons, while **Figure 10** plots the effect sizes of significant features between clusters. Unfortunately, there were no significant differences in terms of outcome variables (**Appendix Table A7**).

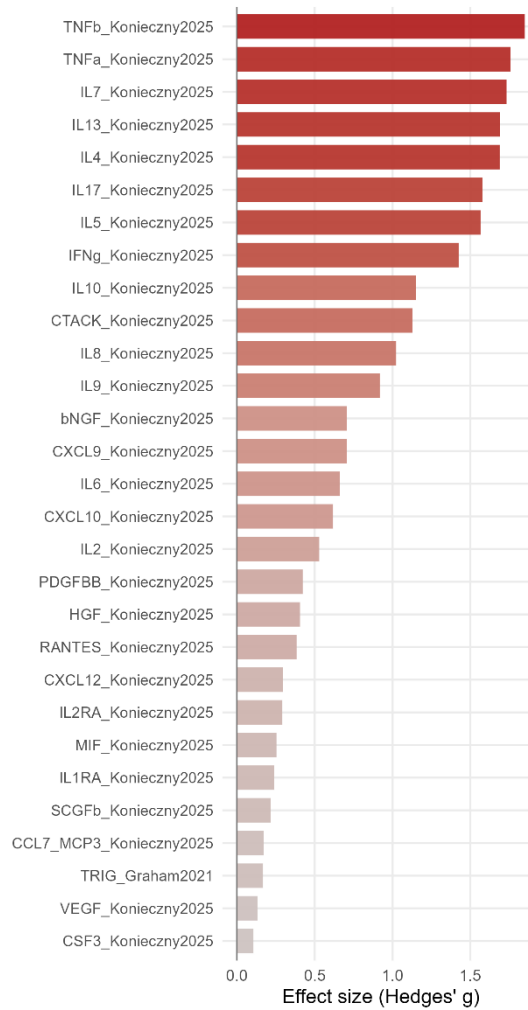


Figure 10. Effect sizes (Hedges' g) of significant input features comparing clusters from the PGS-based stratification model among the MDD sample of the UKB dataset. All positive values (blue) indicate higher values in C10 than in C11.

Finally, the multimodal data-driven stratification, including GM, DTI, rs-fMRI, t-fMRI, and PGSs data, identified 2 significant clusters. One cluster (C11, 47.77%) was characterized by larger surface areas ($q\text{-value}<0.05$), a widespread pattern of reduced

cortical thickness ($q\text{-value}<0.001$), cortical and subcortical volumes ($q\text{-value}<0.001$), FA values ($q\text{-value}<0.001$), and mean activation for the faces condition ($q\text{-value}<0.05$). Moreover, the same cluster showed higher AD ($q\text{-value}<0.001$) and RD ($q\text{-value}<0.001$) values in all white matter tracts, a weaker strength of positive and negative connections in most resting-state networks ($q\text{-value}<0.05$), as well as higher PGSs for MIF ($q\text{-value}<0.047$) and RANTES ($q\text{-value}<0.046$). Remarkably, the wider effect sizes were estimated for RD, FA, and cortical thickness in the same ROIs of the unimodal models, while the resting-state connections showing the highest strength differences belonged to the frontoparietal, dorsal, and ventral attention networks (according to the correspondence reported in **Table 1**). A graphical representation of these comparisons can be found in **Figure 11**, while full statistics are provided in **Appendix Table A5**. Parallely, the same neurobiologically more compromised cluster (C11) also exhibited higher rates of cardiovascular diseases ($q\text{-value}=0.013$) and diabetes ($q\text{-value}=0.021$), and lower motor ($q\text{-value}=0.015$) and processing ($q\text{-value}=0.030$) speed (**Table 13** and **Appendix Table A7**).

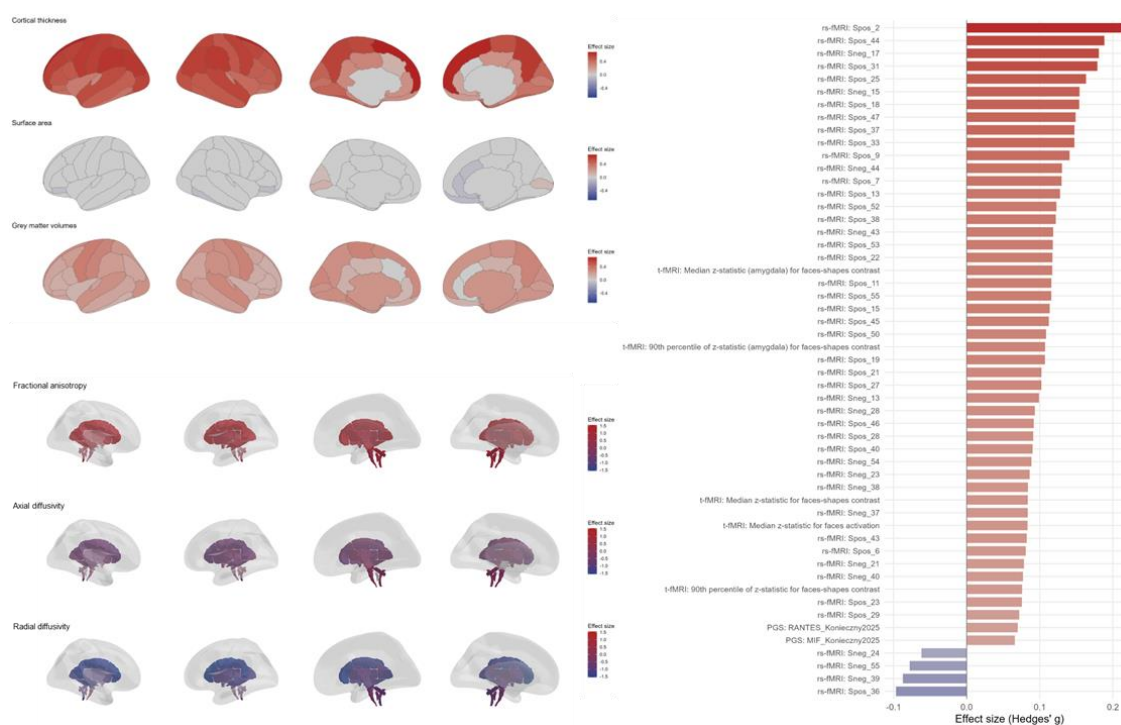


Figure 11. Effect sizes (Hedges' g) of significant input features comparing clusters from the multimodal stratification model among the MDD sample of the UKB dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

Table 13. Significant outcome variable comparisons between clusters resulting from the multimodal stratification model among the MDD sample of UKB.

Variable	C10	C11	Statistic	p-value	q-value
Cardiovascular diseases	0=1755; 1=275	0=1534; 1=323	11.02	0.001	0.013*
Diabetes	0=1997; 1=30	0=1804; 1=51	7.64	0.006	0.021*
Motor speed	566.95 ± 95.45	575.76 ± 98.85	1605457.5	0.003	0.015*
Processing speed	20.93 ± 4.88	20.42 ± 4.79	713138	0.010	0.030*

Abbreviations: Cl, cluster. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

4.1.2.2 Stratification models in the dMDD sample of UKB

In the dMDD sample, all the significant stratification models uncovered 2 distinct and significant clusters. In the clustering model adopting only GM, one cluster (C11, 51.25%) was specifically characterized by a widespread reduction in cortical volumes ($q\text{-value}<0.05$) and cortical thickness ($q\text{-value}<0.001$) in most regions of interest (**Figure 12** and **Appendix Table A6**) with respect to the other cluster (C10). Cortical thickness, in particular, achieved the strongest effect sizes, especially in the bilateral precuneus, the right superior frontal, superior and inferior parietal cortices, and bilateral supramarginal gyrus. The clustering based on DTI revealed a cluster (C10, 44.80%) showing reduced values of FA in all white matter tracts ($q\text{-value}<0.001$), as well as increased AD ($q\text{-value}<0.001$) and RD ($q\text{-value}<0.001$) values in most of the same tracts (**Figure 13** and **Appendix Table A6**). Both FA and RD displayed the largest effect sizes among the anterior, posterior, and superior corona radiata, the corpus callosum, and the superior longitudinal fasciculus. The stratification model yielded by the rs-fMRI data uncovered one cluster (C10, 43.73%) with an extensive reduction in the positive strength of most resting-state networks ($q\text{-value}<0.001$) and mixed results regarding the strength of negative connections ($q\text{-value}<0.05$) among half of the same networks (**Figure 14** and **Appendix Table A6**). The t-fMRI-based model identified one cluster (C10, 32.26%) that showed significantly lower mean activation and habituation levels in both faces ($q\text{-value}<0.001$) and shapes ($q\text{-value}<0.001$) conditions (**Figure 15** and **Appendix Table A6**). Among the clusters that emerged using only PGSs, C10 (45.51%) exhibited significantly higher scores for several inflammatory markers ($q\text{-value}<0.001$), BMI ($q\text{-value}=0.028$), triglycerides ($q\text{-value}=0.002$), and SCZ ($q\text{-value}=0.030$), along with lower

scores for glycated hemoglobin ($q\text{-value}=0.015$) and HDL cholesterol ($q\text{-value}=0.015$) with respect to C11 (**Figure 16** and **Appendix Table A6**). Finally, in the multimodal stratification model, one cluster (C10, 46.59%) was specifically characterized by reduced cortical volumes ($q\text{-value}<0.001$) and thickness ($q\text{-value}<0.001$) in most regions of interest, lower FA values in most white matter tracts ($q\text{-value}<0.001$), as well as higher AD and RD values in several tracts ($q\text{-value}<0.001$), weaker strengths of positive connections among few networks ($q\text{-value}<0.05$), and higher PGS for BD ($q\text{-value}=0.026$). Effect sizes of these comparisons are depicted in **Figure 17** and reported in **Appendix Table A6**, and show that the biggest differences were observed on RD and FA measures within the same white matter tracts as the unimodal DTI-based model.

Despite all these differences identified among input clustering features, and despite some significant differences being observed in terms of depressive symptomatology, motor and processing speed, and BMI, none of the outcome variable comparisons survived FDR correction for the clustering solutions in the dMDD sample (**Table 14** and **Appendix Table A8**).

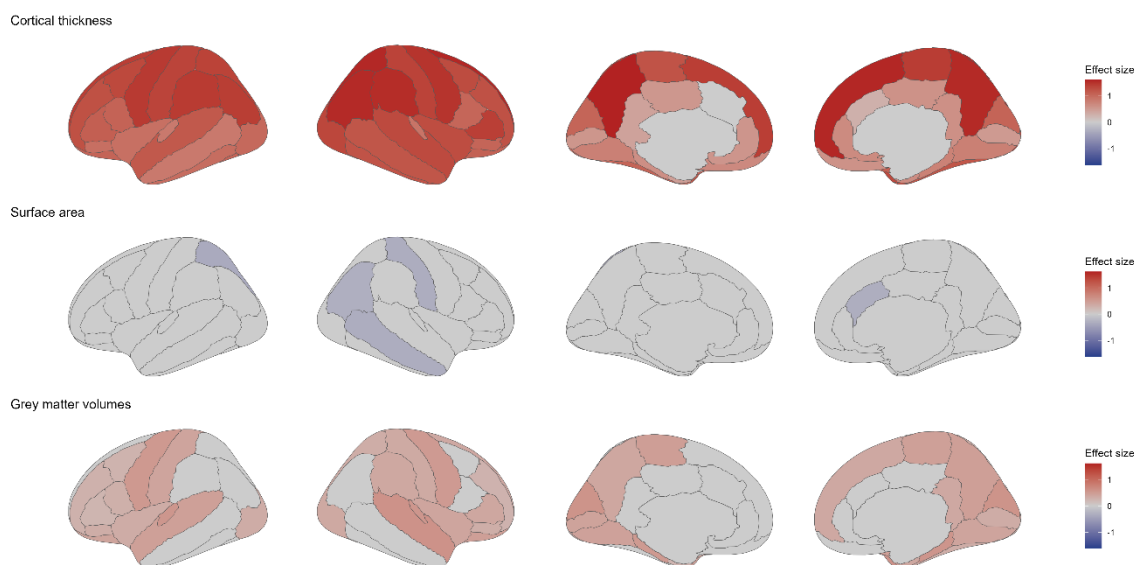


Figure 12. Effect sizes (Hedges' g) of significant input features comparing clusters from the GM-based stratification model among the dMDD sample of the UKB dataset. Positive values (red) indicate higher values for C10 compared to C11, whereas negative values (blue) indicate higher values for C11 compared to C10.

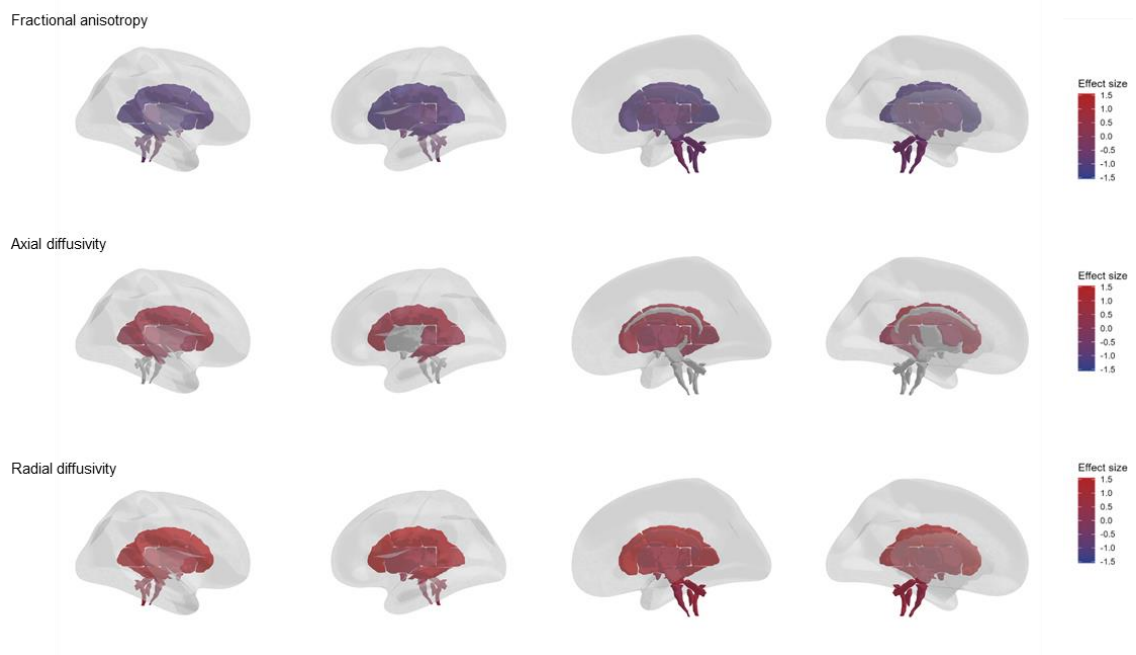


Figure 14. Effect sizes (Hedges' g) of significant input features comparing clusters from the DTI-based stratification model among the dMDD sample of the UKB dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

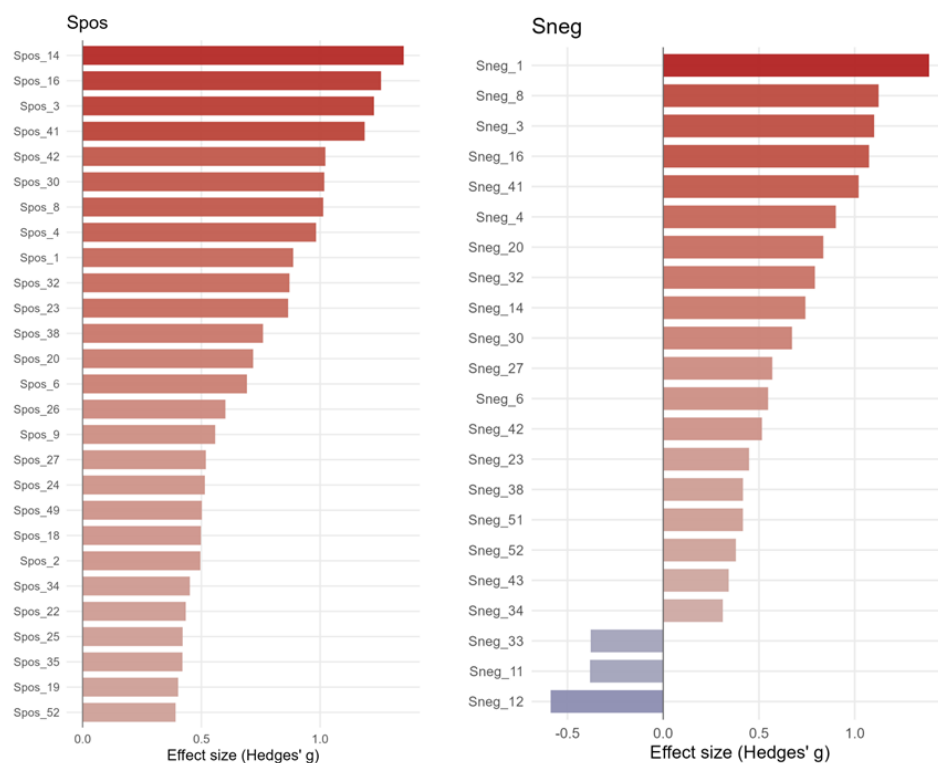


Figure 13. Effect sizes (Hedges' g) of significant input features comparing clusters from the rs-fMRI-based stratification model among the dMDD sample of the UKB dataset. Positive values (red) indicate higher values for C10 compared to C11, whereas negative values (blue) indicate higher values in C11 than in C10.

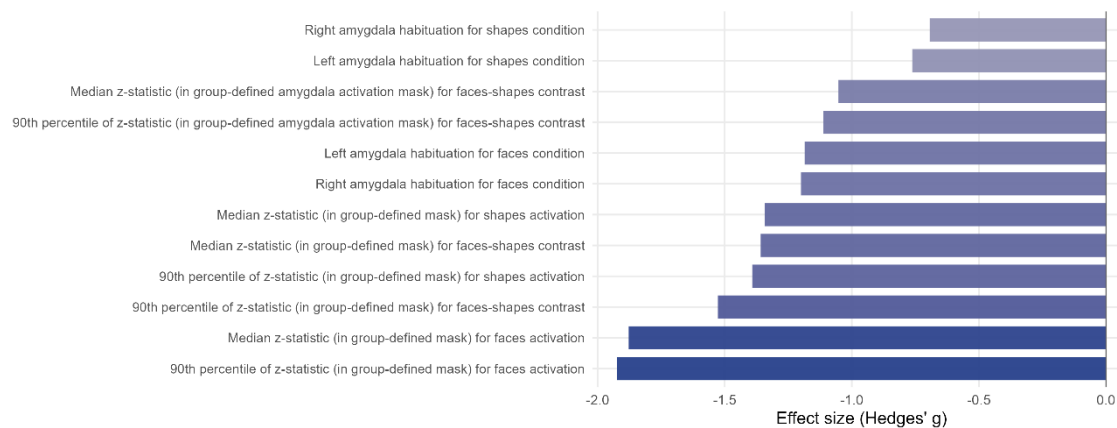


Figure 15. Effect sizes (Hedges' g) of significant input features comparing clusters from the t -fMRI-based stratification model among the dMDD sample of the UKB dataset. All negative values (blue) indicate higher values in C11 than in C10.

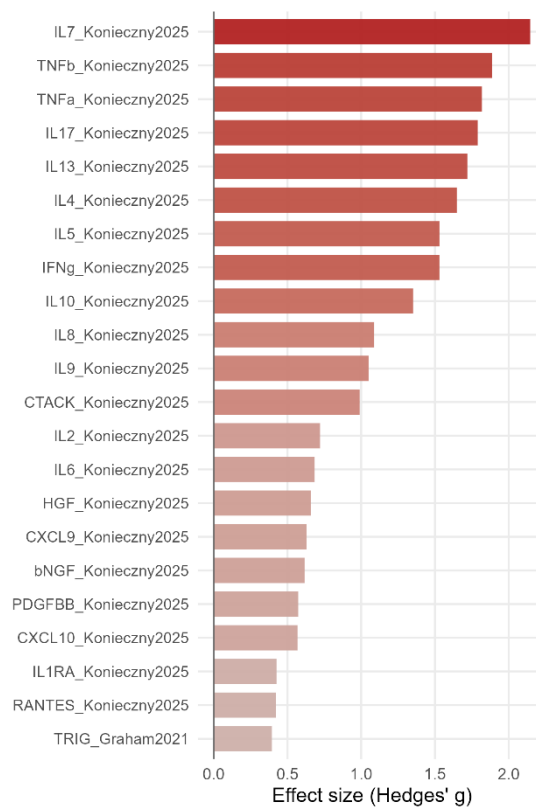


Figure 16. Effect sizes (Hedges' g) of significant input features comparing clusters from the PGS-based stratification model among the dMDD sample of the UKB dataset. All positive values (blue) indicate higher values in C10 than in C11.

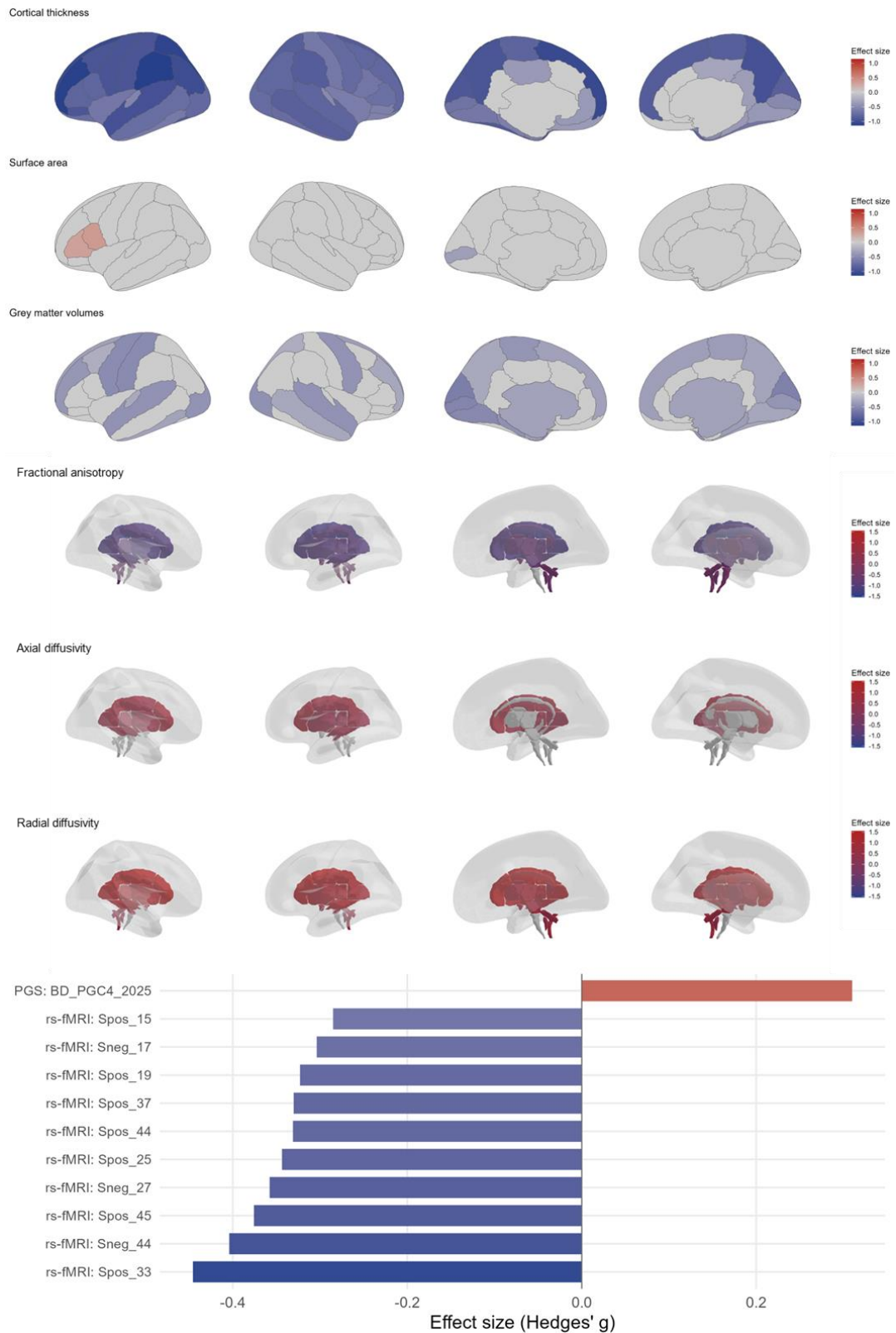


Figure 17. Effect sizes (Hedges' g) of significant input features comparing clusters from the multimodal stratification model among the dMDD sample of the UKB dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

Table 14. Significant outcome variable comparisons between clusters resulting from all significant stratification models among the dMDD sample of UKB.

Stratification model	Variable	CI0	CI1	Statistic	p-value	q-value
GM	Motor speed	563.95 ± 92.10	596.01 ± 119.23	7480.5	0.030	0.212
	Processing speed	21.51 ± 4.64	19.49 ± 6.00	4004.5	0.015	0.211
rs-fMRI	Number of depressive episodes	12.35 ± 27.54	26.83 ± 57.17	422	0.037	0.174
	RDS-4	11.66 ± 1.95	12.10 ± 1.92	8187	0.033	0.174
	PHQ-9	10.44 ± 6.03	12.29 ± 6.63	7647	0.019	0.174
t-fMRI	RDS-4	11.57 ± 1.90	12.07 ± 1.95	7173	0.030	0.254
	BMI	29.07 ± 5.85	27.61 ± 5.83	9825	0.036	0.254
PGSs	RDS-4	12.24 ± 2.07	11.62 ± 1.79	11268	0.013	0.094
	PHQ-9	12.70 ± 6.66	10.45 ± 6.07	11066.5	0.005	0.072
	BMI	28.85 ± 6.30	27.44 ± 5.42	11118.5	0.029	0.135
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	Processing speed	19.49 ± 5.00	21.26 ± 5.68	-2.07	0.040	0.449

Abbreviations: BMI, body mass index; CI, cluster; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI.

4.1.3 Supervised prediction of outcomes

The significant clustering solutions were also used to train elastic-net penalized regression models to predict cluster memberships, as well as the dichotomous outcomes of interest within each cluster. The next paragraphs will provide an overview of the significant predictions for each stratification model among the MDD and dMDD samples of UKB. While all cluster membership predictions' performances are reported in the main text below, full metrics of the outcome variables' predictive models are provided in **Appendix Table A9** for the MDD sample and in **Appendix Table A10** for the dMDD sample.

4.1.3.1 Prediction models in the MDD sample of UKB

All supervised ML models trained to predict cluster memberships reached really high balanced accuracies (BAs), over 95%, with really high significance ($q\text{-value} < 0.001$) across all stratification models (**Table 15**).

Table 15. Cluster membership prediction of significant clustering solutions among the MDD sample of the UKB.

Stratification model	k	BA (%)	AUC	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	2	98.75	1.00	98.63	98.86	<0.001	<0.001*
DTI	2	98.95	1.00	98.25	99.65	<0.001	<0.001*
rs-fMRI	4	90.96	0.99	90.96	96.89	<0.001	<0.001*
t-fMRI	2	96.60	1.00	95.11	98.08	<0.001	<0.001*
PGSs	2	97.97	1.00	97.63	98.30	<0.001	<0.001*
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	2	97.86	1.00	98.28	97.43	<0.001	<0.001*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Regarding the prediction of outcome variables, while diabetes could be significantly predicted by GM, DTI, rs-fMRI, and PGSs modalities in only one cluster, cardiovascular diseases were significantly predicted in two clusters by GM, DTI, and rs-fMRI. Interestingly, these predictions were furtherly enhanced within the multimodal stratification model, whose features were able to significantly predict both diabetes and cardiovascular diseases in both clusters (**Table 16** and **Appendix Table A9**).

Table 16. Significant outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD sample of the UKB.

Stratification model	Variable	Cluster label	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	Diabetes	C10	0.58	58.78	62.07	55.49	0.012	0.036*
	Cardiovascular diseases	C10	0.57	55.26	55.70	54.82	0.003	0.013*
	Cardiovascular diseases	C11	0.57	55.00	53.33	56.66	0.002	0.013*
DTI	Diabetes	C11	0.66	63.89	62.86	64.92	0.001	0.004*
	Cardiovascular diseases	C10	0.62	58.83	57.53	60.13	0.001	0.004*
	Cardiovascular diseases	C11	0.58	54.87	53.85	55.89	0.004	0.012*
rs-fMRI	Diabetes	C12	0.62	65.93	75.00	56.86	0.005	0.042*
	Cardiovascular diseases	C10	0.63	60.53	61.95	59.11	0.001	0.017*

	Cardiovascular diseases	Cl1	0.57	54.69	53.05	56.32	0.021	0.119
PGSs	Diabetes	Cl0	0.69	60.34	63.04	57.64	0.011	0.088
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	Diabetes	Cl0	0.67	63.25	66.67	59.84	0.004	0.012*
	Diabetes	Cl1	0.61	58.42	56.86	59.98	0.021	0.047*
	Cardiovascular diseases	Cl0	0.58	55.45	54.55	56.35	0.002	0.009*
	Cardiovascular diseases	Cl1	0.64	59.58	60.68	58.47	0.001	0.009*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; Cl, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Looking at the bootstrapped coefficients for the multimodal predictive models, a differential contribution of input features within each cluster emerged in the prediction of both diabetes and cardiovascular diseases (**Figures 18 and 19** and **Appendix Tables A11-A14**). Indeed, while the PGS for T2D significantly and positively contributed to the prediction of diabetes in both clusters, diffusivity measures were the top significant negative contributors for diabetes prediction in Cl0, encompassing AD and FA in the corpus callosum and in the right posterior thalamic radiation, as well as FA in the fornix. On the other hand, GM-derived measures mostly contributed to the prediction of diabetes in Cl1, including the volume and area of the lateral orbito-frontal cortex, the mean thickness of the pars opercularis, inferior parietal, superior frontal, and caudal middle-frontal cortices (**Figure 18**). Regarding the prediction of cardiovascular diseases, features from different modalities contributed significantly to the predicted risk in both clusters, yet in Cl1 higher genetic contributions and more brain regions of interest were associated with the outcome (**Figure 19**). For instance, while PGS for T2D significantly fostered the outcome in both clusters, PGSs for IL16 and triglycerides showed significant positive associations with cardiovascular diseases only in Cl1. As concerns neuroimaging measures, a significant positive contribution of AD in the external capsule emerged in both clusters, while a major contribution of AD in the body of the corpus callosum and RD in the body of the corpus callosum and the superior corona radiata was observed only in Cl1. Interestingly, a negative contribution of resting-state connections was detected across clusters, with again more networks being involved in the prediction of cardiovascular diseases in Cl1.

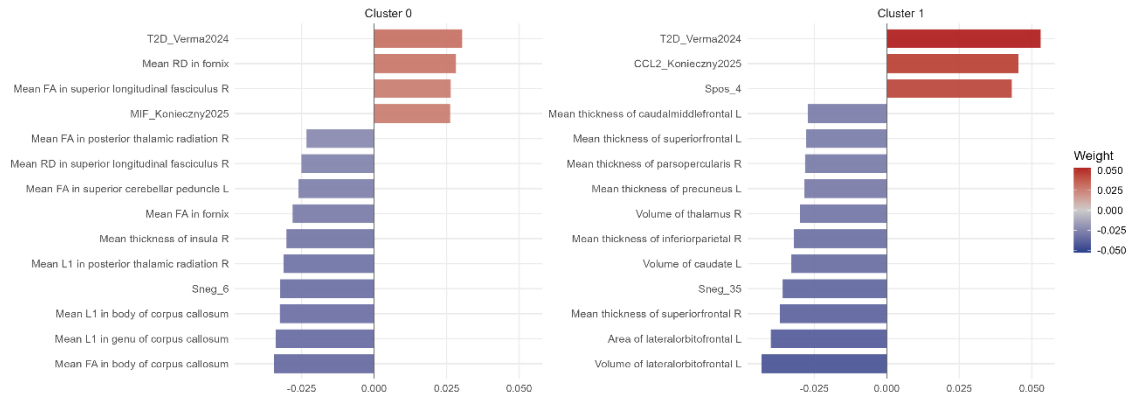


Figure 18. Significant mean bootstrapped coefficients from the elastic net prediction of diabetes in C10 (left) and C11 (right) using features from the multimodal model. Positive values (red) indicate a positive contribution to the outcome, whereas negative values (blue) indicate a negative contribution to the outcome.

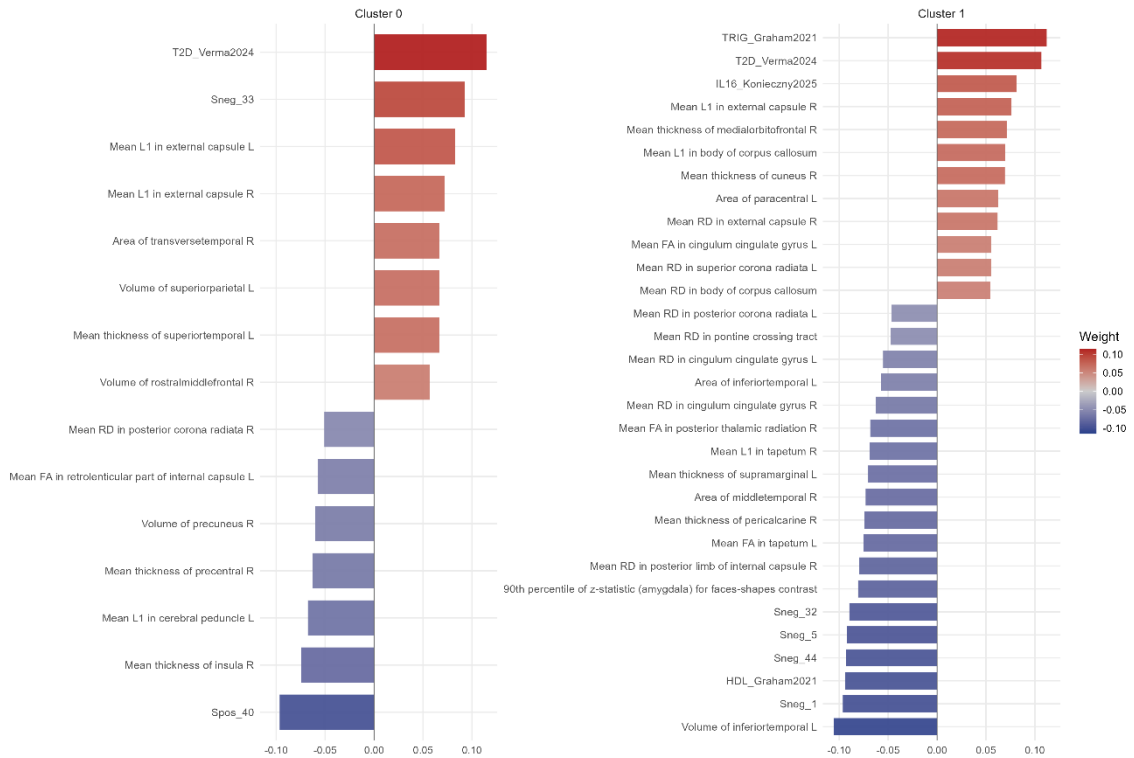


Figure 19. Significant mean bootstrapped coefficients from the elastic net prediction of cardiovascular diseases in C10 (left) and C11 (right) using features from the multimodal model. Positive values (red) indicate a positive contribution to the outcome, whereas negative values (blue) indicate a negative contribution to the outcome.

4.1.3.2 Prediction models in the dMDD sample of UKB

Supervised ML models trained to predict cluster memberships in the dMDD sample were also highly significant ($q\text{-value} < 0.001$), with BAs over 95% and extremely high AUCs across all stratification models (**Table 17**).

Table 17. Cluster membership prediction of significant clustering solutions among the dMDD sample of UKB.

Stratification model	k	BA (%)	AUC	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	2	95.33	0.99	95.80	94.85	<0.001	<0.001*
DTI	2	97.40	1.00	94.81	100.00	<0.001	<0.001*
rs-fMRI	2	96.22	1.00	94.90	97.54	<0.001	<0.001*
t-fMRI	2	97.33	1.00	95.77	98.89	<0.001	<0.001*
PGSs	2	99.34	1.00	98.68	100.00	<0.001	<0.001*
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	2	97.50	1.00	97.79	97.20	<0.001	<0.001*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected p-value (i.e., q-value) < 0.05

As far as the prediction of outcome variables is concerned, t-fMRI data resulted as the only modality being able to survive FDR correction in predicting TRD history in one cluster and self-harming behaviors in both clusters (**Table 18** and **Appendix Table A10**).

Table 18. Significant outcome variables' predictions within each cluster resulting from the significant stratification models among the dMDD sample of the UKB.

Stratification model	Variable	Cluster label	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	Diabetes	Cl1	0.761	72.33	80.00	64.66	0.007	0.056
DTI	Cardiovascular diseases	Cl1	0.656	62.42	67.57	57.26	0.012	0.056
	TRD – history	Cl1	0.604	72.61	80.00	65.22	0.014	0.056
t-fMRI	Ever self-harmed	Cl0	0.67	66.25	61.90	70.59	0.011	0.035*
	Ever self-harmed	Cl1	0.62	62.21	69.44	54.97	0.013	0.035*
	TRD – history	Cl0	0.71	74.63	90.00	59.26	0.008	0.035*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; Cl, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected p-value (i.e., q-value) < 0.05

4.2 Replication analyses on OSR samples

4.2.1 Unsupervised stratification models

Among the OSR datasets, the consensus clustering approach also led to the identification of 2 distinct and significant clusters based on DTI, t-fMRI, and PGSS modalities alone in both samples, that is, the one including patients with MDD (**Table 19**) and the other counting patients with either MDD or BD (**Table 20**). Additionally, the multimodal model combining GM, DTI, rs-fMRI, t-fMRI, and PGSSs reached a statistical significance of $q\text{-value}=0.039$ in the MDD sample.

Regarding the clustering solutions obtained with the dimensionally-reduced features, none of the stratification models were statistically significant (see **Appendix Table A15** and **Appendix Table A16** for detailed statistics of the stratification models on MDD alone and MDD and BD samples, respectively).

Table 19. Summary of consensus clustering models among the MDD sample of OSR.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	Cl0: 5, Cl1: 172	0.59	0.82	0.553
DTI	2	Cl0: 77, Cl1: 81	0.14	2.17	<0.001*
rs-fMRI	3	Cl0: 67, Cl1: 10, 2: 36	0.02	4.54	N.S.
t-fMRI	2	Cl0: 23, Cl1: 59	0.33	1.25	0.003*
PGSSs	2	Cl0: 83, Cl1: 87	0.08	3.13	0.036*
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGS)	2	Cl0: 4, Cl1: 61	0.33	1.31	0.039*

Abbreviations: Cl, cluster; DB, Davies-Bouldin index; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; N.S., not significant; PGSSs, polygenic scores; rs-fMRI, resting-state fMRI; Sil, Silhouette score; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected $p\text{-value}$ (i.e., $q\text{-value}$) < 0.05

Table 20. Summary of consensus clustering models among the MDD and BD sample of OSR.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	Cl0: 156, Cl1: 267	0.16	2.05	0.386
DTI	2	Cl0: 145, Cl1: 199	0.15	2.12	<0.001*
rs-fMRI	2	Cl0: 51, Cl1: 165	0.03	5.30	0.833
t-fMRI	2	Cl0: 78, Cl1: 96	0.27	1.32	<0.001*

PGSs	2	C10: 188, C11: 211	0.07	3.28	0.014*
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGS)	2	C10: 4, C11: 107	0.37	1.21	0.141

Abbreviations: *Cl*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *N.S.*, not significant; *PGSs*, polygenic scores; *rs-fMRI*, resting-state fMRI; *Sil*, Silhouette score; *t-fMRI*, task-based fMRI. *Statistical significance at FDR-corrected *p*-value (i.e., *q*-value) <0.05

4.2.2 Clinical and neurobiological characterization of clusters

4.2.2.1 Stratification models in the MDD sample of OSR

In the stratification model conducted on DTI, which resulted in a significant 2-cluster solution, one cluster (C11, 51.27%) was characterized by decreased values of FA (*q*-value<0.001) in all white matter tracts, along with higher values of RD (*q*-value<0.001) in the majority of tracts, and mixed findings regarding AD values (*q*-value<0.001) in half of the same tracts (see **Figure 20** and **Appendix Table A17**). Most pronounced effect sizes were specifically observed for the bilateral corona radiata, the corpus callosum, and the superior longitudinal fasciculus. The t-fMRI-based clustering solution detected one cluster (C10, 28.05%) with significantly lower mean activation in both faces (*q*-value<0.001) and shapes (*q*-value<0.001) conditions (**Figure 21** and **Appendix Table A17**). Regarding the clusters obtained with PGSs, C11 (51.18%) exhibited significantly higher scores for several inflammatory markers (mostly with a *q*-value<0.001), and CRP (*q*-value=0.026), as well as lower scores for coronary artery disease (*q*-value=0.023) with respect to C10 (**Figure 22** and **Appendix Table A17**). Finally, despite the multimodal stratification model highlighting a significant 2-cluster solution, none of the input features' comparisons were statistically significant after FDR correction (**Appendix Table A17**).

Analogously, even when the clusters were significantly different in terms of input features, and despite some significant differences having been observed in death thoughts and processing speed for the DTI model, and in the number of depressive episodes within the t-fMRI model, none of these comparisons survived the FDR thresholding (**Table 21** and **Appendix Table A18**).

Table 21. Significant outcome variable comparisons between clusters resulting from all significant stratification models among the MDD sample of OSR.

Stratification model	Variable	Cl0	Cl1	Statistic	p-value	q-value
DTI	BDI – item 8	0=37; 1=17; 2=4	0=26; 1=16; 2=11; 3=3	1249	0.018	0.352
	BACS – Processing speed	39.69 ± 14.21	34.89 ± 13.76	3109.5	0.038	0.352
t-fMRI	Number of depressive episodes	7.04 ± 8.19	4.66 ± 4.66	872	0.042	0.476

Abbreviations: BACS, Brief Assessment of Cognition in Schizophrenia; BDI, Beck Depression Inventory; Cl, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; t-fMRI, task-based fMRI.

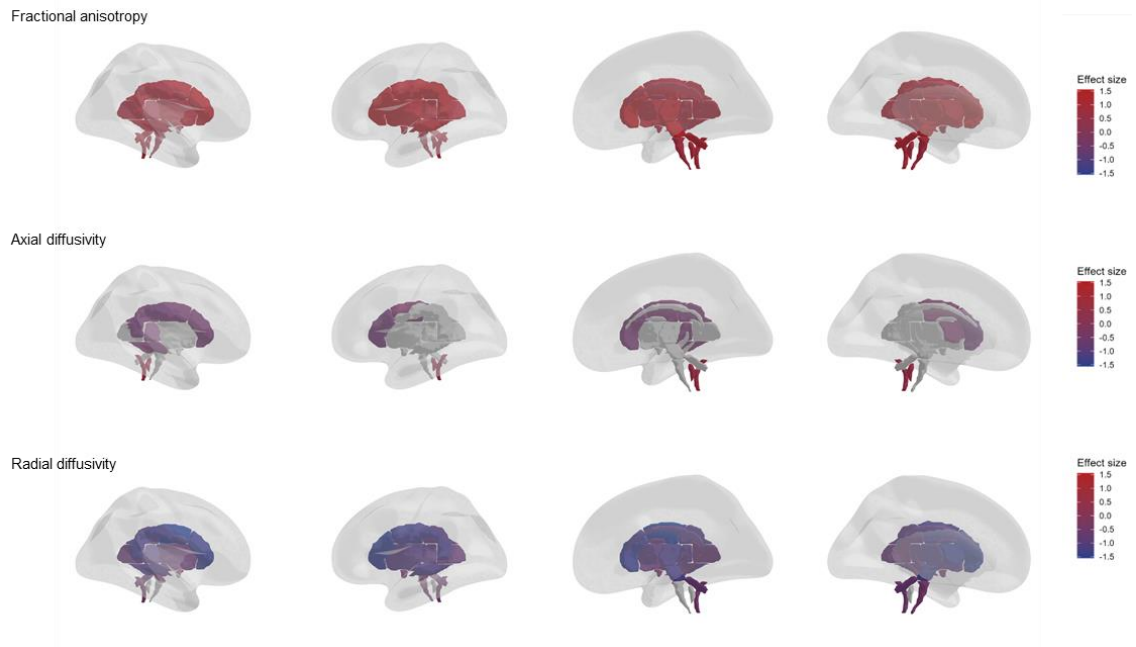


Figure 20. Effect sizes (Hedges' g) of significant input features comparing clusters from the DTI-based stratification model among the MDD sample of the OSR dataset. Positive values (red) indicate higher values for Cl0 compared to Cl1, whereas negative values (blue) indicate higher values for Cl1 compared to Cl0.

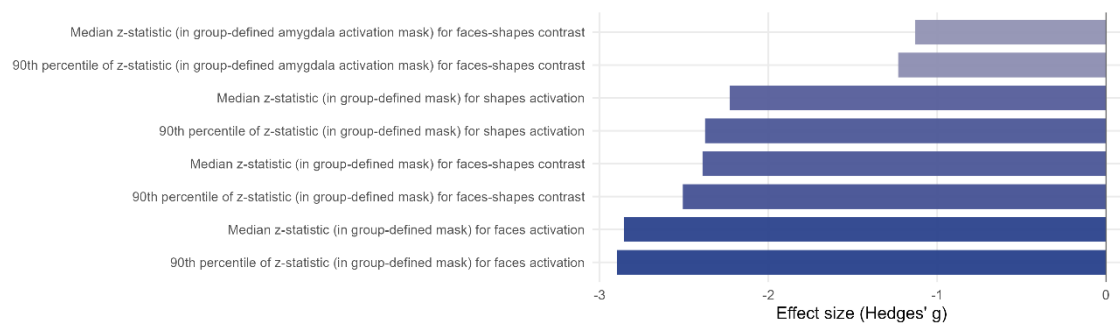


Figure 21. Effect sizes (Hedges' g) of significant input features comparing clusters from the t -fMRI-based stratification model among the MDD sample of the OSR dataset. All negative values (blue) indicate higher values in C11 than in C10.

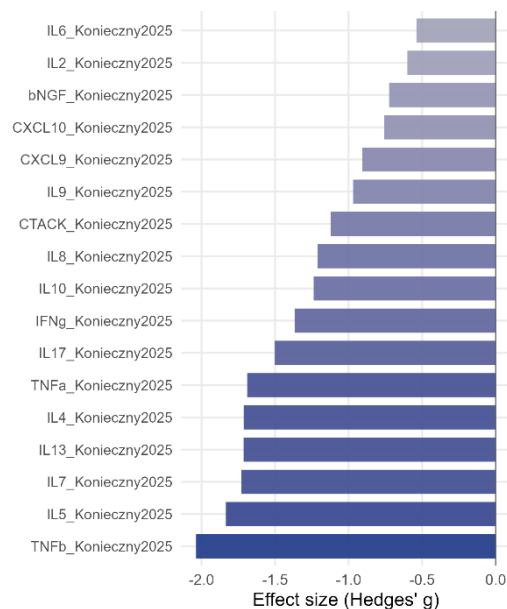


Figure 22. Effect sizes (Hedges' g) of significant input features comparing clusters from the PGS-based stratification model among the MDD sample of the OSR dataset. All negative values (blue) indicate higher values in C11 than in C10.

4.2.2.2 Stratification models in the MDD and BD sample of OSR

Results of the stratification models within the sample with both MDD and BD patients were similar to the MDD sample alone. Indeed, one cluster (C10, 57.85%) that emerged from the DTI stratification was characterized by lower FA (q -value<0.001) and higher RD (q -value<0.001) values in all white matter tracts, while results on AD were mixed, with some tracts showing either significantly increased or decreased diffusivity (Figure 23 and Appendix Table A19). Likewise to the MDD-only cohort, the largest

effect sizes were observed for FA and RD in the corona radiata, corpus callosum, and superior longitudinal fasciculus. Within the t-fMRI clustering solution, one cluster (C11, 55.17%) was again less activated during both faces and shapes conditions, with individuals in the same group also exhibiting lower left ($q\text{-value}=0.019$) and right ($q\text{-value}<0.001$) amygdala habituation measures for the faces condition (**Figure 24** and **Appendix Table A19**). Finally, in the stratification model employing PGSs, the cluster (C11, 52.88%), which had significantly higher scores for several inflammatory markers ($q\text{-value}<0.001$), also showed increased PGSs for CRP ($q\text{-value}<0.001$) and anorexia nervosa ($q\text{-value}<0.001$) with respect to the other group (**Figure 25** and **Appendix Table A19**).

Similar to the results on the OSR MDD sample, no comparisons among outcome variables of interest survived FDR thresholding across these stratification models (**Table 22** and **Appendix Table A20**).

Table 22. Significant outcome variable comparisons between clusters resulting from all significant stratification models among the MDD and BD sample of OSR.

Stratification model	Variable	C10	C11	Statistic	p-value	q-value
DTI	BMI	26.15 ± 4.58	25.14 ± 4.82	16116.5	0.015	0.288
	BACS – Processing speed	34.53 ± 13.73	38.29 ± 13.50	7481.5	0.027	0.288
PGSs	BACS – Verbal memory	37.20 ± 10.76	34.06 ± 10.93	2.605	0.010	0.202

Abbreviations: BACS, Brief Assessment of Cognition in Schizophrenia; BMI, body mass index; Cl, cluster; DTI, diffusion tensor imaging; PGSs, polygenic scores.

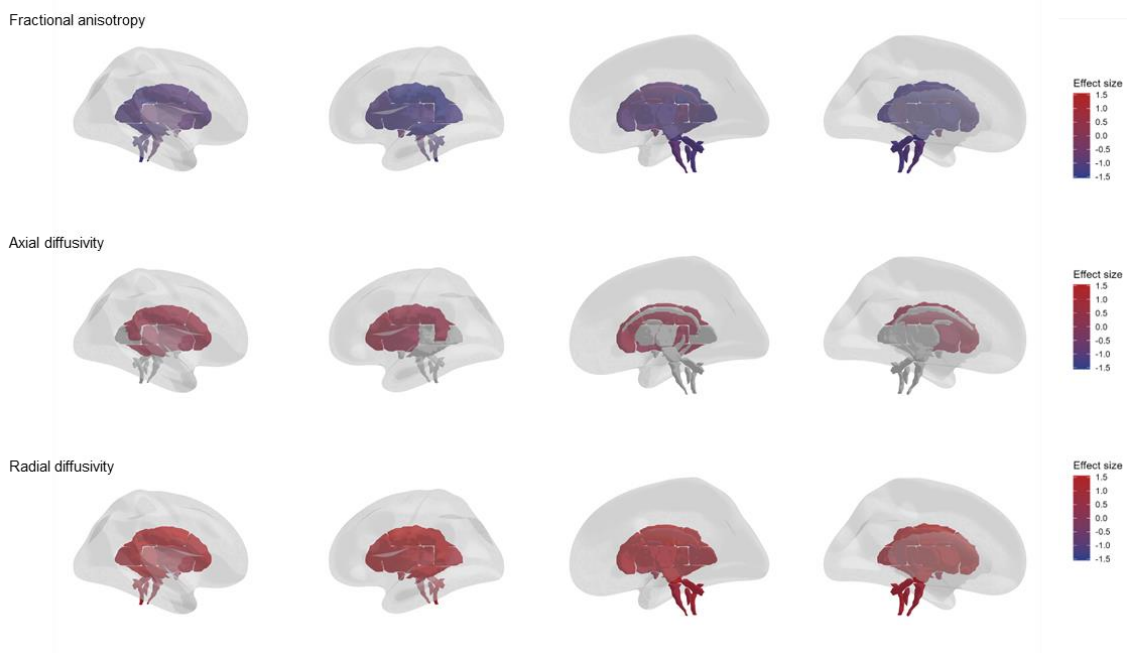


Figure 23. Effect sizes (Hedges' g) of significant input features comparing clusters from the DTI-based stratification model among the MDD and BD sample of the OSR dataset. Positive values (red) indicate higher values in C10 than in C11, whereas negative values (blue) indicate higher values in C11 than in C10.

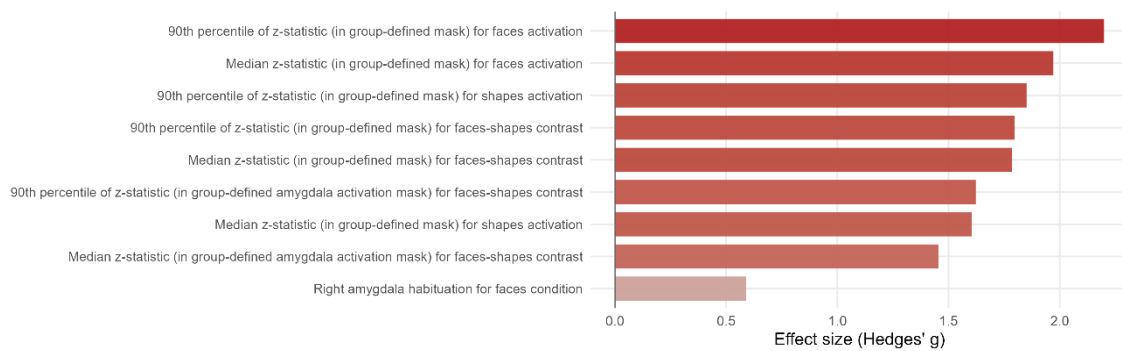


Figure 24. Effect sizes (Hedges' g) of significant input features comparing clusters from the t-fMRI-based stratification model among the MDD and BD sample of the OSR dataset. All positive values (red) indicate higher values in C10 than in C11.

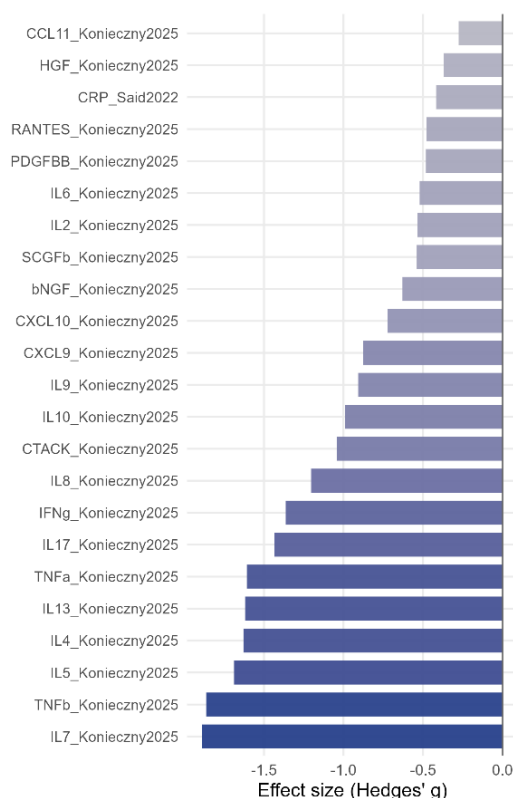


Figure 25. Effect sizes (Hedges' g) of significant input features comparing clusters from the PGS-based stratification model among the MDD and BD sample of the OSR dataset. All negative values (blue) indicate higher values in C11 than in C10.

4.2.3 Supervised prediction of outcomes

As in the main analyses on UKB datasets, the significant clustering solutions obtained within OSR datasets were also used to train elastic-net penalized regression models to predict cluster memberships and the dichotomous outcomes of interest within each cluster. While the performance of all cluster membership predictions and the significant predictive models for the outcome variables are reported in the following paragraphs, full metrics of the outcome variables' predictions are provided in **Appendix Table A21** for the MDD sample and in **Appendix Table A22** for the MDD and BD sample.

4.2.3.1 Prediction models in the MDD sample of OSR

All supervised ML models trained to predict cluster memberships in the MDD sample overcame 90% of BA, paralleled by extremely high AUCs across all significant stratification models (q -value<0.001; **Table 23**).

Table 23. Cluster membership prediction of significant clustering solutions among the MDD sample of the OSR.

Stratification model	k	BA (%)	AUC	Sensitivity (%)	Specificity (%)	p-value	q-value
DTI	2	98.12	1.00	97.53	98.70	<0.001	<0.001*
t-fMRI	2	100	1.00	100	100	<0.001	<0.001*
PGSs	2	93.57	0.99	91.95	95.18	<0.001	<0.001*
Multimodal (GM, DTI, rs-fMRI, t-fMRI, PGSs)	2	100	1.00	100	100	<0.001	<0.001*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

As regards the outcome variables' prediction, the only significant predictive model resulted to be the one predicting cardiovascular disorders with DTI in only one cluster (**Table 24** and **Appendix Table A21**).

Table 24. Significant outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD sample of the OSR.

Stratification model	Variable	Cluster label	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
DTI	Cardiovascular disorders	Cl0	0.77	76.28	83.33	69.23	<0.001	0.008*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; Cl, cluster; DTI, diffusion tensor imaging. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

4.2.3.2 Prediction models in the MDD and BD sample of OSR

In line with the results on the OSR MDD sample, supervised ML models trained to predict cluster memberships for the significant stratification models in the MDD and BD sample also achieved BAs over 95% and high AUCs (p -value<0.001; **Table 25**).

Table 25. Cluster membership prediction of significant clustering solutions among the MDD and BD sample of OSR.

Stratification model	k	BA (%)	AUC	Sensitivity (%)	Specificity (%)	p-value	q-value
DTI	2	97.55	1.00	96.48	98.62	<0.001	<0.001*
t-fMRI	2	97.68	1.00	97.92	97.44	<0.001	<0.001*
PGSs	2	95.50	0.99	95.26	95.74	<0.001	<0.001*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; fMRI, functional magnetic resonance imaging; PGSs, polygenic scores; t-fMRI, task-based fMRI. *Statistical significance at $p\text{-value} < 0.05$

Regarding the prediction of outcome variables, PGSs significantly predicted diabetes in one cluster ($q\text{-value}=0.010$) and, similarly to the UKB dMDD sample, t-fMRI significantly predicted current TRD in one cluster, yet not surviving the FDR correction (Table 26 and Appendix Table A22).

Table 26. Significant outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD and BD sample of OSR.

Stratification model	Variable	Cluster label	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
t-fMRI	TRD – current	C11	0.65	61.61	68.00	55.22	0.042	0.208
PGSs	Diabetes	C11	0.80	79.90	100.00	59.80	0.001	0.010*

Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; Cl, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; t-fMRI, task-based fMRI. *Statistical significance at FDR-corrected $p\text{-value}$ (i.e., $q\text{-value}$) < 0.05

5. Discussion

The current study aimed to assess whether a data-driven approach, informed by multimodal neuroimaging, PGSs, and environmental stressors, could allow for a robust and clinically meaningful stratification of depression. To achieve this, a consensus clustering methodology was successfully applied across two large independent cohorts: a main sample of individuals with lifetime MDD (selected from the UKB) and an independent external replication cohort (recruited at OSR) of hospitalized MDD and BD patients. Beyond stratifying depression based on its neurobiological and environmental signatures, a secondary aim of this project was to assess whether these data-driven clusters would exhibit differential clinical utility, as measured by the prediction of specific health outcomes and medical comorbidities within each subtype.

The analysis first established the existence of replicable biotypes of depression. Robust, data-driven clusters were consistently identified across various single-modality stratification models (i.e., GM, DTI, rs-fMRI, t-fMRI, and PGSs) in the UKB MDD sample, with high internal and external validity, as demonstrated by supervised prediction models achieving BAs exceeding 95%. Remarkably, key neurobiological differences between clusters were replicated in the independent OSR cohort, suggesting the generalizability of the underlying biological structures across different clinical settings.

The central and convergent finding across all stratification models was the identification of a more "neurobiologically compromised" subtype with respect to the others, as particularly evident in the multimodal model in the UKB MDD cohort, which separated the sample into two highly differentiated clusters. One subtype (C11) exhibited a pronounced pattern of neurobiological impairment, characterized by widespread reduced cortical thickness and volume, lower white matter integrity, weaker resting-state functional connectivity, and heightened polygenic risk for inflammatory markers, as compared to the more preserved cluster (C10). This neurobiological profile was strongly and significantly associated with adverse clinical sequelae, including higher rates of cardiovascular diseases, T2D, and poorer motor and processing speed.

Finally, these findings yielded evidence of their clinical and predictive utility. Single-modality predictions provided insights into the strongest associations between the type of input features and specific health outcomes, such as diffusivity measures with cardiovascular risk and PGSs for metabolic and inflammatory traits with diabetes, models

that were replicated in the OSR cohort. Moreover, a novel result emerged from the multimodal prediction in the UKB MDD sample, which demonstrated differential feature contributions on cardiometabolic comorbidities across the identified biotypes. Specifically, the multimodal supervised elastic net model revealed that the most predictive features of an outcome (e.g., diabetes) differed significantly between the clusters, underscoring the need for a precision psychiatry approach where interventions might be tailored to the subtype's underlying biological mechanism.

5.1 Neurobiology-driven stratification of depression identifies replicable and clinically meaningful subtypes

The first objective of the current research project was to identify robust and neurobiologically-informed subtypes of depression, thereby moving beyond the traditional psychiatry nosology based on signs and symptoms. Stratification models were first conducted on several structural and functional neuroimaging modalities, PGSs, and stressful events alone. Then, a multimodal model combining those features that allowed for a significant clustering solution was computed to investigate whether the integration of different sources of heterogeneity in depression would enhance the identification of distinct biotypes. In line with this hypothesis, the multimodal model, including structural neuroimaging (GM, DTI), functional neuroimaging (rs-fMRI, t-fMRI), and PGSs, provided the most comprehensive evidence for two highly distinct subtypes. Indeed, this clustering solution successfully partitioned the lifetime MDD cohort from the UKB into two significant groups, effectively identifying a subgroup of individuals (C11) characterized by widespread neurobiological compromise with respect to the other (C10). This convergence across modalities is critical, as integrated neurobiological alterations are suggested to be essential for defining clinical heterogeneity in complex disorders (Buch & Liston, 2021).

The more “neurobiologically compromised” cluster, in particular, exhibited significant and pervasive reductions across cortical GM and white matter integrity metrics. Specifically, C11 demonstrated a pattern of reduced cortical thickness and volume across most cortical regions compared to C10, with effects particularly pronounced in prefrontal, temporal, and parietal association cortices. The largest

structural effect sizes were observed in the mean thickness of left and right superior and inferior parietal cortices, along with the bilateral precuneus, the supramarginal, and precentral gyri. The superior and inferior parietal lobules (including the supramarginal gyrus) and the precuneus are high-order association hubs interfacing the default-mode, dorsal attention, and frontoparietal networks, which support self-referential cognition, attentional reorienting, and goal-directed control (Kaiser et al., 2015b; Raichle, 2015; Seeley et al., 2007). The concentration of severe atrophy in these high-level processing regions, coupled with significant volume reductions in subcortical structures like the bilateral thalamus and insula, defined a biological signature in line with prior evidence that showed fronto-parietal and paralimbic cortices as consistently implicated in depression. Indeed, in line with our results, previous surface-based and voxel-wise meta-analyses documented both cortical thinning and GM abnormalities among these fronto-parietal regions in MDD (Li et al., 2020; Schmaal et al., 2017; Schmaal et al., 2016; Suh et al., 2019), supporting the idea that association cortices are structurally vulnerable in depression. Subcortically, the thalamus is a relay integrating sensory-cognitive-affective information with strong prefrontal and limbic projections, and its macro- and micro-structural abnormalities that have been reported in MDD were related to cognitive control and mood regulation (Chibaatar et al., 2023; Zhang et al., 2022b). Moreover, the insula, a paralimbic hub of the salience network, showed morphological and functional alterations in depression; this brain area contributes to interoception and affective salience processing, processes that are often disrupted in MDD (Schnellbacher et al., 2022). As mentioned above, the fact that all these regions are key components of the DMN and executive control circuits suggests that this biotype is characterized by a pervasive, large-scale compromise of brain architecture. Both cortical thinning and volume reductions have been hypothesized to result from chronic neurodegenerative processes or persistent neuropathology that can impair the primary cortical substrates of mood and cognition (Moylan et al., 2013), hence contributing to the broad spectrum of emotional, cognitive, and behavioral disturbances observed in MDD, which may be exacerbated in this subtype. In parallel, C11 showed a diffused degradation of white matter microstructure, as evidenced by reduced FA and increased RD and AD across major white matter tracts, especially in the anterior and posterior corona radiata, the corpus callosum, and the superior longitudinal fasciculus. The corona radiata, containing dense projection fibers

linking frontal and parietal cortices with the thalamus and brainstem, underpins executive control, attention, and motor functions (Drevets et al., 2008). Large meta-analyses in MDD previously reported robust FA reductions and diffusivity increases in these pathways, consistent with disrupted fronto-subcortical communication (Liao et al., 2013; van Velzen et al., 2020). Altered integrity of the corpus callosum, which is the principal interhemispheric commissure, has also been repeatedly described in depression and linked to impaired interhemispheric integration, psychomotor slowing, and emotion regulation abnormalities (Bubb et al., 2018; van Velzen et al., 2020; Wise et al., 2016). Finally, diffusion abnormalities in the superior longitudinal fasciculus, which connects dorsolateral prefrontal, inferior parietal, and superior temporal association cortices (i.e., core nodes of the frontoparietal and dorsal attention networks that support working memory and cognitive control), have been associated with cognitive and attentional inefficiency in MDD (Chen et al., 2016; van Velzen et al., 2020). Functionally, integrity across these long-range highways is crucial for processing speed and large-scale network efficiency (Bullock et al., 2022). Therefore, elevations in RD, typically interpreted as evidence of demyelination or loss of oligodendrocytes, along with increased AD and FA reductions, which may indicate axonal and extracellular water alterations (Alexander et al., 2011; Winklewski et al., 2018), provide plausible underpinnings for the slowed motor and processing speed characteristic of the more-compromised subtype (Penke et al., 2010; Turken et al., 2008; Winklewski et al., 2018). These alterations may result from the cumulative effects of stress on brain structure, as chronic glucocorticoid release and stress-related neuroinflammation can severely affect structural axonal integrity (Abraham et al., 2022). Hence, these findings are in line with previous studies proposing decreased FA and increased RD in the same white matter pathways as key mechanisms in the etiopathogenesis of the most severe forms of depression (Shen et al., 2017; van Velzen et al., 2020).

From a functional perspective, the more-compromised subtype was further distinguished by weaker positive and negative resting-state connections in several networks, as well as a general trend toward reduced t-fMRI activation to emotional and non-emotional stimuli compared to the less-compromised CI0. Specifically, the resting-state connections that showed the higher effect sizes primarily belonged to the frontoparietal, ventral, and dorsal attention networks, which are respectively involved in

flexible executive control and working memory, top-down goal-directed orienting and sustained visuo-spatial attention, and stimulus-driven salience detection of events (Cole et al., 2013; Seeley et al., 2007), and whose connectivity has been found to be impaired in depression (Kaiser et al., 2015b). On the one hand, the reduced strength of both positive and negative functional resting-state connectivity across these control and attention networks indicates reduced large-scale integration and control efficiency, supporting the hypothesis of a “connectome landscape of dysconnectivity” as a transdiagnostic etiological factor contributing to major psychiatric disorders (Fornito et al., 2015; van den Heuvel & Sporns, 2019). Critically, it converges with the same structural disconnection patterns suggested by white matter disruptions detected with DTI (i.e., reduced FA and increased RD in long-range tracts), reinforcing a systems-level dysconnectivity mechanism in which microstructural damage and network-level dysfunction jointly contribute to the more-compromised MDD phenotype (Liao et al., 2013; van Velzen et al., 2020). On the other hand, these results are slightly in contrast with classic models of depression emphasizing limbic hyperreactivity (Drevets et al., 2008; Hamilton et al., 2012), and instead point to a subtype with relative functional task-evoked hypoactivation. Nevertheless, these features are compatible with affect/cognitive inefficiency and consistent with meta-analytic demonstrations of large-scale network imbalance and heterogeneous limbic responsivity in MDD (Groenewold et al., 2013; Kaiser et al., 2015b), thereby possibly denoting a specific depression subtype characterized by emotional blunting or melancholic features linked to functional hypoactivation (Foti et al., 2014; Fountoulakis et al., 2004; Kustubayeva et al., 2023). Taken together, the convergence of structural atrophy, white matter damage, and functional hypo-connection and activation suggests a large-scale disruption of brain integrity at several neurobiological levels, marking this subtype as the most severely affected biotype identified.

The neurobiological profile of the more-compromised subtype was also characterized by genetic correlates potentially predisposing individuals towards inflammatory and metabolic dysregulations. Indeed, this cluster showed significantly higher PGSs for macrophage migration inhibitory factor (MIF) and the regulated on activation, normal T-cell expressed and secreted (RANTES). Both MIF and RANTES are key chemokines involved in neuroinflammation (Leighton et al., 2018; Milenkovic et al.,

2019), suggesting that a portion of the neurobiological alterations observed in C11 might be driven by a heightened genetic susceptibility to inflammatory processes (Milaneschi et al., 2020). In line with this, prior studies implicated MIF and RANTES in MDD pathophysiology, symptom severity, and cognition, supporting broader links between chemokine signaling and mood disorders (Bauer et al., 2020; Małujło-Balcerska et al., 2022; Petralia et al., 2020; Supti et al., 2023). Indeed, the higher genetic susceptibility for inflammatory markers may lead to an increased vulnerability to stressors, hence resulting in heightened stress-related neuroinflammatory responses, in turn affecting brain functional and structural integrity (Beurel et al., 2020). Moreover, these genetic underpinnings specifically characterizing the more “neurobiologically compromised” cluster align with the concept of the so-called “immuno-metabolic depression”, a clinically relevant and distinct depression subtype characterized by inflammatory and metabolic dysregulations, atypical neurovegetative symptoms, and higher cardiometabolic risk (Milaneschi et al., 2020; Penninx et al., 2025).

Consistent with the immuno-metabolic subtype hypothesis, the identified neurobiological correlates were paralleled by significant differences in the cardiometabolic comorbidities of the more-compromised cluster. Indeed, C11 had significantly higher odds of co-occurring cardiovascular diseases ($q\text{-value}=0.009$) and T2D ($q\text{-value}=0.047$), marking it as a high-risk group for somatic diseases, which have been widely associated with an increased risk of mortality and treatment resistance in depression (Berk et al., 2023; Weir & Rapaport, 2022). This finding reinforces the idea that severe MDD, and specifically the immune-related phenotype of depression, can be considered a systemic illness characterized by overlapping neuro-vascular and neuro-metabolic pathophysiology that further complicates the subtype’s prognosis (Milaneschi et al., 2020; Penninx et al., 2025; Taylor et al., 2013).

Finally, the widespread neurobiological alterations in C11 were accompanied by cognitive performance deficits, specifically by poorer motor speed ($q\text{-value}=0.015$) and processing speed ($q\text{-value}=0.030$). This neurocognitive profile is mechanistically plausible given the tract-wide alterations of the diffusion metrics. Indeed, since processing speed is closely dependent on the integrity of white matter pathways and their conduction efficiency (Penke et al., 2010; Turken et al., 2008), this outcome provides

robust behavioral validation that the microstructural white matter damage observed in C11 (i.e., reduced FA and increased RD) results in measurable functional impairment.

Considering all these findings together, our results are in line and suggest a plausible explanation for the compromise observed in one of the two identified subtypes. Indeed, a genetic predisposition towards inflammatory processes may lead to a heightened risk for severe somatic comorbidities and heightened neuroinflammatory stress-related responses that may affect both structural and functional brain integrity, which can, in turn, serve as a mediator of cognitive performance (Fanelli et al., 2022).

While the multimodal analysis provided the most holistic picture, single-modality models effectively confirmed these core findings, highlighting the robustness of the detected heterogeneity dissection. For instance, in the unimodal GM clustering, a more-compromised GM cluster was strongly characterized by reduced cortical thickness in regions such as the superior frontal gyrus and inferior parietal cortex. Clinically, this GM biotype was significantly associated with diabetes ($q\text{-value}=0.036$), echoing the association found in the multimodal solution. This strong link between cortical thinning in executive and limbic regulation circuits and diabetes is consistent with previous studies suggesting that GM alterations in the medial prefrontal cortex are associated with disrupted glucose metabolism pathways (Cao et al., 2024; Moran et al., 2013; Zhang et al., 2022a; Zhao et al., 2022). The DTI model identified a subtype again defined by pervasive reduced FA and increased RD across major white matter tracts. This microstructural pathology was significantly linked to an increased risk of cardiovascular diseases ($q\text{-value}=0.004$). This association is biologically meaningful, as small vessel disease (i.e., a common cause of white matter lesions) and cardiovascular diseases share vascular risk factors that compromise white matter integrity, which may parallelly contribute to the psychiatric pathology (Abraham et al., 2016; Fang et al., 2020; Tuladhar et al., 2015). The unimodal stratification model based on t-fMRI also replicated the finding of a functional hypoactivation to emotional and non-emotional stimuli. This functional deficit was associated with increased depressive symptomatology (RDS-4, $q\text{-value}=0.033$), higher cardiovascular risk ($q\text{-value}=0.008$), and significantly impaired processing speed ($q\text{-value}=0.004$). The association between functional hypoactivation and poor processing speed, along with the findings from the DTI-based model, suggests that the functional activation is strongly dependent on the health of the underlying white

matter pathways that facilitate processing speed (Honey et al., 2009; Marstaller et al., 2016; Zheng et al., 2018). Therefore, these findings robustly link this functional phenotype to the more-compromised DTI and structural biotypes, as also confirmed by the multimodal stratification model. Moreover, the unimodal PGSs model identified a cluster with high polygenic liability for several inflammatory cytokines, notably tumor necrosis factor β (TNF- β), interleukin (IL) 13, and IL-4, which are implicated in the immune dysregulation observed in MDD (Köhler et al., 2017; Osimo et al., 2020). This genetic risk converged also on cardiometabolic traits, given that the same cluster showed significantly higher PGSs for BMI, CRP, and T2D, along with lower PGS for HDL cholesterol. These findings support the role of the genetic liability for inflammatory and metabolic factors as a distinct, underlying axis of MDD heterogeneity (Milaneschi et al., 2020; Milaneschi et al., 2017), and suggest a substantial role of these markers in contributing to the immune-metabolic phenotype of depression.

The generalizability of these neurobiological signatures was first tested in a smaller, clinical sub-sample ($n=279$) of currently depressed individuals (i.e., dMDD) selected from the UKB dataset. In this sample, the clustering solutions consistently reproduced the underlying pattern of neurobiological compromise found in the larger lifetime MDD cohort. Indeed, one distinct cluster across the unimodal and multimodal solutions consistently exhibited widespread patterns of reduced cortical volumes and thickness, lower FA, higher RD, weaker positive resting-state connectivity, and decreased functional task-based activations. The PGSs model in the dMDD sample similarly identified an inflammatory biotype characterized by significantly higher PGSs for multiple inflammatory markers. The reproducibility of this neurobiological differentiation across the two UKB samples suggests the identified biotypes are stable constructs, transcending illness state (i.e., lifetime vs. current). However, consistent with expectations for smaller cohorts, none of the clinical outcomes (including cardiometabolic risk or cognitive performance differences) survived FDR correction in the dMDD sample. This failure to confirm differential outcomes is highly likely a consequence of reduced statistical power, potentially compounded by the more acute and homogenous severity of currently depressed individuals, masking subtle long-term comorbidity effects (Marek & Laumann, 2024).

The external and transdiagnostic validity of the identified biotypes was further tested on an independent cohort of depressed MDD and BD inpatients from OSR. While some of the consensus clustering solutions did not reach statistical significance in the OSR sample due to cluster size limitations, direct feature comparisons of the significant unimodal stratifications revealed that core neurobiological alterations were successfully replicated. Specifically, key features of the more-compromised biotype were observed in the OSR MDD sample, including clusters exhibiting significantly lower FA and increased RD in major white matter tracts (e.g., anterior corona radiata and body of the corpus callosum). Furthermore, the core functional deficit (i.e., reduced t-fMRI activation to faces and shapes stimuli) was strongly pronounced in OSR, with effect sizes often exceeding those observed in the UKB. The increased magnitude of effect sizes specifically observed for this modality within the MDD cohort of hospitalized patients underscores the importance of including t-fMRI measures for an accurate stratification (Tozzi et al., 2024), thereby prompting the emotional activation correlates as fundamental biomarkers to stratify depression, especially during its acute illness phases.

The inclusion of the BD patients within the OSR sample allowed us to consider the transdiagnostic relevance of these biotypes. Our results show that the type of structural alterations (e.g., lower FA and higher RD in the DTI-based model) is similar in BD and MDD, although differences in specific brain regions may exist (Xu et al., 2024). The fact that the functional and structural biotypes observed in OSR were characterized by the same directional deficits (e.g., lower FA and reduced t-fMRI activation) as in UKB suggests that the neurobiological taxonomy identified here may represent a transdiagnostic dimension of severe mood disorder, rather than a distinction specific to MDD versus BD.

As regards the results on the dimensionally-reduced datasets, most stratification models did not reach statistical significance among both UKB and OSR datasets, except for the stress-based models. These findings suggest that merging continuous variables, such as the neuroimaging-derived measures, into latent components may have removed variance from the original data, thereby removing the individual variability that is fundamental for an efficient stratification (Lippitt et al., 2024). On the other hand, PCA on categorical data, such as the features regarding ACEs and SLEs, may be useful to

identify continuous latent scores that can enhance the computational efficiency of clustering algorithms (Jensen et al., 2024; Stannard et al., 2024).

5.2 Supervised prediction of clinical outcomes uncovers a differential contribution of neurobiological correlates

The integration of unsupervised clustering with supervised ML provided a crucial step beyond mere classification by demonstrating the clinical utility and predictive power of the identified biotypes (Liang et al., 2020; Marquand et al., 2016). By training models to predict not only cluster membership but also relevant clinical outcomes within each cluster, we uncovered differential pathways of risk, a step critical to move psychiatry towards a precision medicine perspective (Bzdok & Meyer-Lindenberg, 2018).

A key finding supporting the reliability and distinctiveness of the identified biotypes in the UKB cohort was the remarkably high performance achieved in predicting cluster membership. Indeed, across nearly all unimodal and multimodal stratification models, supervised prediction using a cross-validated elastic net framework yielded BAs over 95% and AUCs approaching 100%. This extremely high predictive performance confirmed that the input biological features could successfully delineate distinct, non-overlapping subgroups within the MDD population, and provides the possibility of applying these models to new patients – without re-training algorithms – to assess their risk of belonging to a specific cluster with high reliability (Varoquaux et al., 2018). Furthermore, this result validated the initial unsupervised consensus clustering approach, establishing that the neurobiological signatures defining these clusters were sufficiently robust to serve as stable biomarkers for patient stratification (Buch & Liston, 2021).

In the wide UKB MDD cohort, while single-modality models successfully predicted specific outcomes in at least one cluster (e.g., GM, DTI, and rs-fMRI predicted cardiovascular diseases; DTI, rs-fMRI, and PGSs predicted diabetes), the multimodal model was the only one capable of significantly predicting both diabetes and cardiovascular diseases in both the less-compromised (C10) and the more-compromised (C11) clusters. This result underscores the importance of combining diverse biological information, confirming that chronic somatic risk in MDD is unlikely attributable to a single pathophysiological mechanism but rather emerges from a converged, system-wide

vulnerability profile captured effectively only by multimodal analysis (Buch & Liston, 2021). The most novel implication for personalized treatment stemmed from the analysis of differential feature contribution within these supervised models. This revealed that the biological mechanisms driving a specific comorbidity greatly differed between the two MDD biotypes.

In the more “neurobiologically compromised” cluster (C11), the genetic predisposition was the most influential risk factor for comorbid diabetes, with the PGS for T2D (Verma et al., 2024) exhibiting the largest positive weight among all significant predictors. This T2D PGS contributed to the outcome alongside the PGS for the chemokine CCL2 (Konieczny et al., 2025), supporting a genetically-driven risk profile marked by metabolic and inflammatory vulnerability. Previous studies showed that the CCL2/CCR2 axis is implicated in T2D pathophysiology (Pan et al., 2021), as it promotes monocyte trafficking and microglial activation, processes that can sustain cortical neuroinflammation in depressive disorders (Curzytek & Leśkiewicz, 2021). In line with this, within this more-compromised cluster, the strongest negative weights – interpretable as protective factors – were reached by cortical structural metrics, particularly the mean thickness of superior frontal and caudal/middle frontal cortices, as well as the volume of the right thalamus and left caudate. These findings suggest that, in this subgroup, preserved integrity of executive and subcortical regions moderates the risk for diabetes, in line with prior neuroimaging research showing that T2D and insulin resistance are associated with cortical thinning and subcortical atrophy (Cao et al., 2024; Zhang et al., 2022a), also in depressed individuals (Ajilore et al., 2010). Since central insulin action in prefrontal and subcortical circuits regulates systemic metabolism, cortical/subcortical alterations may exacerbate glycemic dysregulation, whereas preservation of these regions may be protective (Moran et al., 2013). Conversely, in the less-compromised cluster (C10), while the T2D PGS (Verma et al., 2024) also emerged as a top risk predictor, paralleled by a positive influence of the MIF PGS (Konieczny et al., 2025), diabetes was significantly and negatively predicted by white-matter integrity measures, such as FA and AD in the corpus callosum, hence suggesting a different etiopathological contribution to metabolic dysfunction in this cluster. This pattern aligns with meta-analytic evidence suggesting an association between T2D and widespread reductions in FA, and with studies linking poorer white matter integrity to worse metabolic status (Huang et al.,

2021; Zhou et al., 2021). Interestingly, in line with our findings, a previous study on UKB also found a significant association with the PGS for T2D and reduced global FA, which was particularly evident among MDD-related fronto-temporo-parietal connections (Repple et al., 2022). Cytokines such as MIF have been previously associated with insulin resistance and cardiometabolic disease in both preclinical and clinical studies (Kleemann & Bucala, 2010; Morrison & Kleemann, 2015), providing a plausible link between genetic liability (i.e., MIF PGS), metabolic dysfunction, and white matter integrity. Indeed, MIF is an upstream innate-immune mediator mainly produced by adipose tissue, whose experimental inhibition or genetic deficiency has been shown to improve insulin sensitivity and glycemic control in preclinical models (Kleemann & Bucala, 2010; Morrison & Kleemann, 2015). In this context, better-preserved callosal integrity may maintain interhemispheric conduction efficiency and large-scale network coupling (Hoogenboom et al., 2014), thereby mitigating the behavioral and physiological cascades (e.g., reduced activity, cognitive slowing, autonomic dysregulation) that exacerbate insulin resistance in the presence of putative MIF-related inflammatory stress (Kullmann et al., 2020).

Beyond the heightened risk for diabetes, the more-compromised cluster (C11) displayed a cardiovascular risk profile in which inherited metabolic and inflammatory liability was prominent. The largest positive predictive weights were carried by PGSs for triglycerides (Graham et al., 2021), T2D (Verma et al., 2024), and the cytokine IL-16 (Konieczny et al., 2025), indicating that metabolic dysfunctions and low-grade inflammation can be major determinants of cardiovascular diseases in this biotype, in line with the immuno-metabolic phenotype of depression linking metabolic traits to cardiometabolic outcomes (Milaneschi et al., 2017). In line with this profile, neurobiological compromise remained a significant risk contributor. Indeed, diffusion metrics reflecting white matter microstructural damage, specifically higher AD and RD in the external capsule and body of the corpus callosum, also showed significant positive weights. These tracts have been shown to be those most sensitive to cerebral small-vessel disease (Croall et al., 2017; Pasi et al., 2016; Yang et al., 2024), such that DTI abnormalities in these regions have been demonstrated to predict vascular risk and vascular events beyond conventional MRI markers (Evans et al., 2016; VandeBunte et al., 2023). In parallel, functional measures emerged as protective contributors in C11.

Specifically, greater strength of negative resting-state network connections (i.e., stronger anticorrelations across several networks) and higher task-evoked amygdala responses to faces versus shapes were associated with lower cardiovascular risk. This pattern is plausible given that small-vessel disease is characterized by reduced structural and functional network efficiency and connectivity, whereas preserved functional coupling is linked to better vascular–brain health (Boot et al., 2020; Lawrence et al., 2014; Schulz et al., 2021; Zhang et al., 2024). Moreover, spontaneous neural activity and task-based responsiveness are tightly dependent on intact neurovascular coupling, which is impaired by vascular risk and inflammation, so that preserved activation may reflect resilience of the vascular–neuronal interface (Meyer-Baese et al., 2025). In the less-compromised cluster (C10), the T2D PGS (Verma et al., 2024) again emerged as a positive predictor of comorbid cardiovascular disorders, accompanied by white-matter indices, including higher AD in the bilateral external capsule. However, a sparser set of predictors reached a significant weight in the model, possibly because the overall neurobiological variance was narrower, leaving fewer independent predictors that survived penalization (Varoquaux, 2018). The consistent involvement of diffusion metrics across both clusters supports the idea that subtle white-matter damage, often secondary to microvascular pathology, represents a transdiagnostic endophenotype of cardiovascular risk that is detectable with DTI (Evans et al., 2016; Pasi et al., 2016).

Considering both outcomes' prediction, the patterns observed in C11 point to a cardiometabolic–inflammatory pathway contributing to both metabolic and cardiovascular risks, with a polygenic liability for metabolic and inflammatory traits being a shared driver of risk, while brain structural integrity and function can modulate how that liability can express on a phenotypic level. In a personalized medicine perspective, tailored strategies for C11 may prioritize the management of the metabolic and inflammatory burden, opting for treatments aimed at reducing inflammation, thereby compensating for the genetic susceptibility to heightened inflammation. Indeed, beyond traditional pharmacological treatments, preventive anti-inflammatory strategies, including healthy lifestyle, physical exercise, and diet, can act as neuroprotective agents and mitigate vascular burden (Paolucci et al., 2018; Phillips & Fahimi, 2018), thereby preserving white matter integrity and favoring an efficient resting-state connectivity (Zhao et al., 2020), which, according to our findings, can counteract cardiometabolic

outcomes and can serve as risk monitors. Moreover, given that the same more-compromised cluster was significantly associated with poorer processing and motor speed, individuals belonging to this subtype might benefit from tailored cognitive remediation strategies, which are effective techniques for cognitive deficits in depression (Legemaat et al., 2021) and are also shown to promote neuroplasticity (Morimoto et al., 2012; Morimoto et al., 2014), furtherly improving white matter diffusivity and large-scale functional connectivity (Chapman et al., 2015; Shu et al., 2022). In line with these considerations, our results highlight the importance of biotype-tailored prevention and treatment strategies, integrating polygenic profiling with white matter and functional imaging markers to select optimal targets and track response.

While the UKB MDD sample provided the most comprehensive predictive models for somatic comorbidities, the analysis of the currently depressed UKB sub-sample provided specific insights into the predictive value of acute functional states. Indeed, despite being statistically underpowered to survive FDR correction, the t-fMRI model, capturing differences in affective processing, yielded significant predictions for outcomes related to acute severity and poor response, including self-harming behaviors and a history of TRD. In line with the recent work by Tozzi et al. (2024) underscoring the importance of including task-based activations for an accurate patient stratification, our model suggests that functional imaging metrics, such as functional hypoactivation during emotional processing, may be highly sensitive, state-dependent markers of severe or melancholic depression, often linked to suicidal ideation and resistance to conventional pharmacotherapy (Kustubayeva et al., 2023; Lorenzo-Luaces et al., 2021; Miola et al., 2023; Vieira et al., 2023; Williams et al., 2015).

Results from the predictive models tested in the OSR samples provided a crucial test of their generalizability. Despite the smaller sample size, the models showed partial replication of the features linked to cardiometabolic risk observed in UKB. For example, the DTI model in the OSR MDD sample significantly predicted cardiovascular disorders in one identified subtype, with FA and RD in the splenium of the corpus callosum and the superior corona radiata emerging as the top contributors. This finding replicated results from both DTI and multimodal models within the UKB MDD dataset, supporting the idea that white matter integrity can be a reliable and translatable biomarker for vascular risk across various clinical settings. Additionally, the PGSs model in the

transdiagnostic OSR sample (including both MDD and BD) significantly predicted diabetes in one cluster, with PGS for CCL2 (Konieczny et al., 2025) again being detected as one of the main significant predictors. The ability of polygenic inflammatory risk scores to predict metabolic outcomes across MDD and BD aligns with growing evidence that immuno-genetic, inflammatory, and metabolic factors are transdiagnostic dimensions of vulnerability in severe mood disorders (Milaneschi et al., 2020; Penninx et al., 2025; Poletti et al., 2024; Vancampfort et al., 2015). Lastly, the strongest predictive value of t-fMRI in the MDD and BD groups was in predicting treatment resistance during the current depressive episode among patients in the more-compromised cluster, replicating the same finding of the UKB dMDD sample. This t-fMRI profile, marked by a reduced activation in response to emotional stimuli, is often associated with melancholic features and may serve as an endophenotype, highly predictive of poor treatment response (Godlewska et al., 2018; Kotoula et al., 2023; Williams et al., 2015). This specific predictive result emphasizes the potential of t-fMRI metrics to detect functionally severe, treatment-relevant brain states that need clinical attention, regardless of long-term physical outcomes (Pilmeyer et al., 2022).

The successful replication of these predictive links in the independent OSR cohort, particularly in the t-fMRI, PGSs, and DTI modalities, supports their cross-sample generalizability and confirms that these neurobiological markers may be useful in clinical practice for a robust and transdiagnostic cardiometabolic risk profiling in depression.

5.3 Strengths and limitations

The current research project advances data-driven neurobiological stratification of depression in several ways. First, to the best of our knowledge, this is the earliest large-scale study to integrate multimodal MRI (i.e., GM, DTI, rs-fMRI, and t-fMRI) with PGSs for several psychiatric disorders, cardiometabolic-related conditions, and inflammatory markers to derive and externally validate biotypes of depression. The integration of several and distinct sources of heterogeneity allowed for a comprehensive stratification capturing complex interactions across different pathways and mechanisms involved in the etiopathogenesis of depression (Buch & Liston, 2021). By conducting our main analysis in an extensive epidemiological cohort of individuals with lifetime MDD (i.e., UKB) and replicating key findings in a large external clinical sample of hospitalized

MDD and BD patients (i.e., OSR), we assessed the generalizability of findings across clinical settings (i.e., general population and inpatient) and in a transdiagnostic context. The overall design of the current work directly addressed common limitations of previous studies that relied on single-modality features, modest samples, and no out-of-sample testing (Beijers et al., 2019; Marquand et al., 2016; Miranda et al., 2021). Therefore, by explicitly examining the convergence across neurobiological modalities and the generalizability across settings, this study provided a more ecological and valid dissection of depression heterogeneity.

From a methodological standpoint, implementing a consensus clustering approach allowed us to identify stable, robust, and reproducible subgroup structures. Indeed, this methodology aggregates over resamplings to reduce algorithm- and initialization-dependence and to quantify clustering stability (Monti et al., 2003). Clusters' validity was then tested both statistically, by ensuring that the identified subgroups significantly represented distinct entities rather than being random partitions of a single distribution (Huang et al., 2015), and clinically, by demonstrating that those clusters were not only characterized by diverse neurobiological profiles (e.g., diffuse DTI abnormalities, cortical thinning, and functional hypoactivation), but also paralleled by differential cardiometabolic risk and cognitive profiles. This dual validation supports the conclusion that the resulting subtypes were clinically meaningful, not merely mathematical partitions. In addition, the use of standardized UKB imaging pipelines to process neuroimaging enhanced reproducibility and comparability of measures across cohorts (Alfaro-Almagro et al., 2018). These choices align with best-practice recommendations for transparent, reproducible neuroimaging, including standardized preprocessing, code and data sharing, and thorough reporting (Nichols et al., 2017; Poldrack et al., 2017).

Another novel contribution of this work regards the combination of unsupervised ML with complementary supervised prediction models. On the one hand, the predictive models speak to the potential translational applicability of the identified subtypes. Indeed, the use of a cross-validation framework allowed us to estimate the out-of-sample generalizability and transportability of findings beyond the discovery cohort (Scheinost et al., 2019; Varoquaux, 2018), thereby outlining a feasible tool to support clinical risk assessment, such as estimating the probability that an individual with depression belongs to a given subtype or will develop severe somatic comorbidities, engage in self-harming

behaviors, or fail to respond to first-line treatments (Gao et al., 2018; Lee et al., 2021). On the other hand, the supervised models yielded modality-specific insights into how neurobiological and genetic features relate to metabolic and cardiovascular outcomes, revealing possible biotype-specific etiopathogenetic pathways (e.g., CCL2 liability modulated by GM preservation vs. MIF liability modulated by white matter integrity) and highlighting t-fMRI as a state-sensitive predictor of treatment resistance in currently depressed patients.

Finally, the transdiagnostic inclusion of MDD and BD in the OSR cohort aligns with dimensional frameworks (e.g., RDoC), supporting the idea that immuno-metabolic and neurocircuit dimensions cut across categorical diagnoses and may better track clinical outcomes than diagnostic labels alone (Cuthbert, 2022; Insel, 2014).

Along with the above-mentioned advantages, some limitations of this work should be acknowledged. For instance, external validation was qualitative rather than quantitative, since models developed in UKB were not directly transported unchanged to OSR and, instead, model calibration and fitting were re-estimated within the OSR dataset. Therefore, this approach did not constitute a strict test of transportability of the original UKB models (i.e., applying the fixed model to new data, with performance assessed out-of-sample), and limited the generalizability of the specific UKB parameter estimates. Nevertheless, qualitative replication, re-deriving the same feature-outcome patterns under different populations and measurement conditions, still informed methodological robustness, indicating that the underlying signals and stratification framework were stable across settings. Although we replicated core findings (e.g., an immune-metabolic subtype identified across settings, DTI contributions to cardiovascular risk, cortical thinning associated with diabetes, and t-fMRI predicting treatment resistance), some effects did not survive stringent FDR correction in OSR. On the one hand, this failure to replicate some stratification models could reflect reduced statistical power due to cluster size limitations. On the other hand, context differences between a broad, population-based UKB cohort and a more homogeneous, severely depressed, and hospitalized clinical sample may have contributed. Indeed, consistent with prior work, inpatient or current-episode MDD samples are often deliberately recruited as homogeneous clinical cohorts (Fugger et al., 2020; Zimmerman et al., 2002), adopting restrictive inclusion and exclusion criteria that reduce heterogeneity (Zetin & Hoepner, 2007; Zimmerman et al.,

2004). In contrast, population-based lifetime MDD cohorts, such as the one present in the UKB, encompass broader variability and clinically heterogeneous depression definitions (Davis et al., 2020; Howard et al., 2020; Jermy et al., 2021), which likely dilute effect sizes and increase variance relative to hospitalized or current-episode samples. Regarding cross-cohort differences, pharmacological treatment should also be mentioned. Indeed, while not all individuals in the UKB dataset ever took an antidepressant medication during their lifetime, all OSR patients were currently undergoing pharmacological treatments, which are known to affect both brain structure and function (Dusi et al., 2015; Harmer et al., 2017), thereby possibly introducing a bias when trying to replicate neurobiology-outcomes associations. In addition, the ancestry composition of both cohorts (i.e., predominantly European in the UKB cohort and Italian in the OSR samples) also limited the generalizability of findings to other ethnicities. PGS models, in particular, are known to exhibit ancestry-dependent performance, and their clinical deployment without adequate diversity may exacerbate health-care disparities (Martin et al., 2019; Sirugo et al., 2019).

From a practical implementation perspective, MRI data is resource-intensive and not universally accessible, which can hamper the immediate clinical translation of current findings. Indeed, despite growing interest in lower-cost MRI solutions, cost and infrastructure barriers remain critical (Arnold et al., 2023; Liu et al., 2021). In line with this, future studies should employ more scalable, cost-effective markers (e.g., socio-demographics, electronic health records, laboratory tests, or peripheral inflammatory markers) to validate the currently identified depression subtypes, and hence assess whether they could serve as pragmatic proxies for biotype assignment and risk prediction.

The cross-sectional nature of the current research also represents a limitation for its clinical application, as it does not reflect the dynamic nature of mood disorders, thereby hampering the detection of illness trajectories over time (Rhebergen et al., 2012).

Finally, a further design consideration concerns the lack of healthy controls. While adding healthy individuals can highlight disease-control contrasts, including them in an unsupervised framework can trivialize clustering by separating cases vs. controls rather than unraveling within-MDD heterogeneity. Therefore, our case-only clustering was preferable for dissecting intra-diagnostic patterns (Coombes et al., 2021). However, including healthy controls in a stratification study may have a double utility: on the one

hand, if healthy controls are included in the clustering analysis, it may help to identify reliable biomarkers that can support the detection of high-risk individuals, promote screening, and design early preventive strategies; on the other hand, a control group could be helpful to compare the detected clusters of patients to healthy subjects, assessing the degree of neurobiological alterations identified for each subtype.

To overcome these limitations, future stratification studies should (i) pursue quantitative replications in large multi-site and multi-ethnic samples, including non-European ancestries; (ii) evaluate cost-effective markers of the brain-genetic signatures – such as peripheral inflammatory panels (e.g., CRP, IL-6, neutrophil-to-lymphocyte ratio, chemokines), metabolic biomarkers, behavioral phenotypes – to predict cluster membership and outcome risk, and assess clinical utility of the identified clusters where MRI is infeasible; (iii) test biotype-matched interventions (e.g., cardiometabolic risk management, anti-inflammatory strategies, cognitive remediation, physical exercise) in prospective, stratified trials; (iv) validate the stratification models on longitudinal data, for instance to predict conversion to chronic MDD, TRD, or comorbidity development, hence assessing the prognostic value of these subtypes; (v) compare the neurobiological signatures of the identified clusters to a healthy control group, to evaluate the degree of neurobiological compromise characterizing each subtype; and (vi) adopt transparent, shareable workflows to facilitate cross-cohort and independent re-analysis (Poldrack et al., 2017). Together, these steps will move the field from biologically grounded stratification toward clinically actionable precision psychiatry.

5.4 Clinical and research implications of the current study

The results obtained by the present study carry critical implications for both clinical practice and future research directions. The data-driven identification of two stable biotypes, one of which was specifically characterized by a widespread pattern of neurobiological compromise paralleled by a heightened risk of cardiometabolic comorbidities and cognitive impairment with respect to the other, underlines the need for moving beyond traditional diagnostic categories. Current DSM-5-TR and ICD-11 psychiatric classification systems aggregate heterogeneous patients who markedly differ in symptom presentations, illness trajectories, structural and functional neurobiological correlates, and immuno-metabolic markers, limiting the precision and effectiveness of

treatment selection (Cuthbert, 2022; Insel, 2014). In this sense, an ML-based and biologically-informed stratification could help clinicians' decision-making about optimal treatment strategies, reducing reliance on a "trial-and-error" approach, which contributes to the risk of relapsing and complicates remission (Buch & Liston, 2021; DeRubeis et al., 2014). In this context, multimodal integration is essential. Indeed, our multimodal stratification model, combining different sources of neurobiological heterogeneity, has provided the most comprehensive solution, capturing variance that single modalities missed, and offering more accurate insights into the etiopathogenetic complexity of depression.

The identified more "neurobiologically compromised" biotype of depression in our multimodal stratification may serve as a candidate endophenotype for translational work. Its converging signatures, comprising fronto-parietal cortical thinning, callosal diffusivity disruptions, weaker resting-state connectivity, reduced task-evoked responses, and elevated inflammatory PGSs, offer an objective substrate that does not rely solely on subjective symptom reports and that aligns with contemporary views of immuno-metabolic depression (Milaneschi et al., 2020; Penninx et al., 2025), prompting a new conceptualization of depression that should not be overlooked by clinical theoretical approaches or by future research designs. In parallel, functional markers of acute state, particularly t-fMRI indices of hypoactivation during emotional processing, showed predictive value for self-harm risk and treatment resistance in currently depressed patients, converging with evidence that task-evoked activation patterns can stratify melancholic and severe depression presentations and forecast antidepressant outcomes (Ichikawa et al., 2020; Kustubayeva et al., 2023; Miola et al., 2023; Williams et al., 2015). Pragmatically, the assessment of these functional indices could help to identify possibly at-risk patients needing an early, effective, and tailored management, such as adjunctive non-pharmacological interventions (e.g., neuromodulation, psychotherapy) when state severity is high (Gerlach et al., 2022; Riera-Serra et al., 2024; Vai et al., 2023).

Our predictive models further provided insights into differential etiopathogenetic mechanisms contributing to cardiometabolic risk in the identified subtypes. For instance, while polygenic liability for metabolic-inflammatory traits was a shared driver of diabetes and cardiovascular outcomes, brain integrity seemed to have a modulating effect on phenotypic expression. In the more-compromised cluster, risk was characterized by a

cardiometabolic-inflammatory pathway, as delineated by a positive contribution of T2D, triglycerides, and CCL2 PGSs, amplified by diffuse white-matter alterations. Conversely, preserved functional coupling and task responsivity appeared to be protective, consistent with models linking small-vessel disease to network inefficiency and worse outcomes (Lawrence et al., 2014; Schulz et al., 2021). In a clinical context, these mechanisms call for a dual-targeted preventive strategy, targeting systemic cardiometabolic and inflammatory aspects and reinforcing brain vulnerability. For instance, this subtype may benefit from a rigorous management of vascular and metabolic risk (including hypertension, dyslipidemia, smoking, and obesity), anti-inflammatory strategies where appropriate, and neuroprotective lifestyle interventions to preserve white matter integrity and network efficiency, including physical exercise and cognitive remediation (Boot et al., 2020; Chapman et al., 2015; Milaneschi et al., 2020; Paolucci et al., 2018; Pasi et al., 2016; Penninx et al., 2025; Phillips & Fahimi, 2018; Shu et al., 2022).

Future research should design studies taking into account these considerations. First, a multimodal approach should be prioritized to avoid missing critical levels of information. Moreover, a longitudinal design would be essential to establish the prognostic value of the identified clusters, thereby assessing whether individuals belonging to the more-compromised subtype show higher-risk trajectories toward TRD, vascular dementia, or increased mortality. Prospective monitoring should integrate state markers (e.g., t-fMRI) with integrity markers (e.g., DTI and cortical thickness) to track the cardiometabolic risk. In addition, randomized controlled trials should be stratified and test for biotype-matched interventions, using imaging and clinical outcomes as additional endpoints (Kapur et al., 2012; Milaneschi et al., 2020; Penninx et al., 2025; Woo et al., 2017). Furthermore, integrating molecular markers, such as peripheral immune panels, transcriptomics, and metabolomics, can further refine mechanisms underlying the more-compromised biotype and yield scalable proxies where MRI is impractical (Buch & Liston, 2021). Finally, studies should move from qualitative to quantitative external validation across ancestries and settings, and provide transparent and transportable methodologies, in line with best practices for study replication and clinical prediction (Collins et al., 2015; Nichols et al., 2017; Poldrack et al., 2017).

5.5 Conclusions

In conclusion, this dissertation significantly advances and makes a step forward in the context of mood disorders' stratification and the precision psychiatry framework. Indeed, our findings demonstrate that depression can be meaningfully stratified into neurobiologically defined subtypes with distinct risk profiles and clinical relevance. By integrating multimodal information and replicating analyses on external cohorts, we identified a robust, stable, and highly characterized more-compromised biotype with respect to the other, marked by convergent cortical thinning, widespread white-matter alterations, functional resting-state and affective hypoactivation, and increased polygenic liability for metabolic-inflammatory traits, paralleled by a heightened risk for severe somatic comorbidities and cognitive dysfunction. Remarkably, this subtype converges with contemporary immuno-metabolic models of depression. Combining unsupervised data-driven models with supervised ML, these signatures generalized and provided sufficient information to predict cardiometabolic comorbidities and treatment resistance within each subtype, highlighting complementary roles for polygenic scores, diffusion imaging, and task-evoked functional measures. Together, these findings move beyond symptom-based categories to a framework in which multimodal brain integrity and genetic liability jointly shape prognosis, and in which biotype membership can guide targeted prevention (e.g., metabolic and vascular risk control, anti-inflammatory strategies) and early, state-sensitive interventions (e.g., neuromodulation or cognitive remediation when functional compromise is prominent). In sum, this research establishes a reproducible, multimodal groundwork for a personalized medicine approach for depression, prompting biologically informed subtyping as the practical path to more accurate risk stratification, more optimal treatment selection, and ultimately, better outcomes.

References

- Aas M, Henry C, Andreassen OA, Bellivier F, Melle I, Etain B (2016) The role of childhood trauma in bipolar disorders. *International journal of bipolar disorders* 4: 2
- Abraham HM, Wolfson L, Moscufo N, Guttmann CR, Kaplan RF, White WB (2016) Cardiovascular risk factors and small vessel disease of the brain: Blood pressure, white matter lesions, and functional decline in older persons. *Journal of cerebral blood flow and metabolism : official journal of the International Society of Cerebral Blood Flow and Metabolism* 36: 132-142
- Abraham M, Mundorf A, Brodmann K, Freund N (2022) Unraveling the mystery of white matter in depression: A translational perspective on recent advances. *Brain and behavior* 12: e2629
- Ahmed YB, Al-Bzour AN, Alzghoul SM, Ibrahim RB, Al-Khalili AA, Al-Majali GN, Hamza AI, Al-Zamer YS, Alhayek K, Kofahi R *et al* (2023) Limbic and cortical regions as functional biomarkers associated with emotion regulation in bipolar disorder: A meta-analysis of neuroimaging studies. *Journal of affective disorders* 323: 506-513
- Ajilore O, Narr K, Rosenthal J, Pham D, Hamilton L, Watari K, Elderkin-Thompson V, Darwin C, Toga A, Kumar A (2010) Regional cortical gray matter thickness differences associated with type 2 diabetes and major depression. *Psychiatry research* 184: 63-70
- Alexander AL, Hurley SA, Samsonov AA, Adluru N, Hosseinbor AP, Mossahebi P, Tromp do PM, Zakszewski E, Field AS (2011) Characterization of cerebral white matter properties using quantitative magnetic resonance imaging stains. *Brain connectivity* 1: 423-446
- Alfaro-Almagro F, Jenkinson M, Bangerter NK, Andersson JLR, Griffanti L, Douaud G, Sotiropoulos SN, Jbabdi S, Hernandez-Fernandez M, Vallee E *et al* (2018) Image processing and Quality Control for the first 10,000 brain imaging datasets from UK Biobank. *NeuroImage* 166: 400-424
- Allen N, Sudlow C, Downey P, Peakman T, Danesh J, Elliott P, Gallacher J, Green J, Matthews P, Pell J (2012) UK Biobank: Current status and what it means for epidemiology. *Health Policy Technology* 1: 123-126

- Alloy LB, Olino T, Freed RD, Nusslock R (2016) Role of Reward Sensitivity and Processing in Major Depressive and Bipolar Spectrum Disorders. *Behavior therapy* 47: 600-621
- Alshehri T, Mook-Kanamori DO, Willems van Dijk K, Dinga R, Penninx B, Rosendaal FR, le Cessie S, Milaneschi Y (2023) Metabolomics dissection of depression heterogeneity and related cardiometabolic risk. *Psychological medicine* 53: 248-257
- Altshuler LL, Bartzokis G, Grieder T, Curran J, Jimenez T, Leight K, Wilkins J, Gerner R, Mintz J (2000) An MRI study of temporal lobe structures in men with bipolar disorder or schizophrenia. *Biological psychiatry* 48: 147-162
- American Psychiatric Association (2022) *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision*. American Psychiatric Association
- Aminoff SR, Tesli M, Bettella F, Aas M, Lagerberg TV, Djurovic S, Andreassen OA, Melle I (2015) Polygenic risk scores in bipolar disorder subgroups. *Journal of affective disorders* 183: 310-314
- Amstadter AB, Maes HH, Sheerin CM, Myers JM, Kendler KS (2016) The relationship between genetic and environmental influences on resilience and on common internalizing and externalizing psychiatric disorders. *Social psychiatry and psychiatric epidemiology* 51: 669-678
- Andersson JLR, Jenkinson M, Smith S (2007a) Non-linear optimisation. FMRIB technical report TR07JA1. *Practice*
- Andersson JLR, Jenkinson M, Smith S (2007b) Non-linear registration, aka Spatial normalisation FMRIB technical report TR07JA2. *FMRIB Analysis Group of the University of Oxford* 2
- Andersson JLR, Sotiropoulos SN (2015) Non-parametric representation and prediction of single- and multi-shell diffusion-weighted MRI data using Gaussian processes. *NeuroImage* 122: 166-176
- Andersson JLR, Sotiropoulos SN (2016) An integrated approach to correction for off-resonance effects and subject movement in diffusion MR imaging. *NeuroImage* 125: 1063-1078
- Andreassen OA, Hindley GFL, Frei O, Smeland OB (2023) New insights from the last decade of research in psychiatric genetics: discoveries, challenges and clinical

- implications. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 22: 4-24
- Anselmetti S, Poletti S, Ermoli E, Bechi M, Cappa S, Venneri A, Smeraldi E, Cavallaro R (2008) The Brief Assessment of Cognition in Schizophrenia. Normative data for the Italian population. *Neurological sciences : official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology* 29: 85-92
- Arnaud AM, Brister TS, Duckworth K, Foxworth P, Fulwider T, Suthoff ED, Werneburg B, Aleksanderek I, Reinhart ML (2022) Impact of Major Depressive Disorder on Comorbidities: A Systematic Literature Review. *The Journal of clinical psychiatry* 83
- Arnold TC, Freeman CW, Litt B, Stein JM (2023) Low-field MRI: Clinical promise and challenges. *Journal of magnetic resonance imaging : JMRI* 57: 25-44
- Av Kák Kollsker S, Coello K, Stanislaus S, Melbye S, Lie Kjaerstad H, Stefanie Ormstrup Sletved K, Vedel Kessing L, Vinberg M (2022) Association between lifetime and recent stressful life events and the early course and psychopathology in patients with newly diagnosed bipolar disorder, first-degree unaffected relatives and healthy controls: Cross-sectional results from a prospective study. *Bipolar disorders* 24: 59-68
- Barysheva M, Jahanshad N, Foland-Ross L, Altshuler LL, Thompson PM (2013) White matter microstructural abnormalities in bipolar disorder: A whole brain diffusion tensor imaging study. *NeuroImage Clinical* 2: 558-568
- Bauer O, Milenkovic VM, Hilbert S, Sarubin N, Weigl J, Bahr LM, Wetter TC, Heckel B, Wetzel CH, Rupprecht R *et al* (2020) Association of Chemokine (C-C Motif) Receptor 5 and Ligand 5 with Recovery from Major Depressive Disorder and Related Neurocognitive Impairment. *Neuroimmunomodulation* 27: 152-162
- Beck AT, Beck RW (1972) Screening depressed patients in family practice: A rapid technic. *Postgraduate medicine* 52: 81-85
- Beckmann CF, Smith SM (2004) Probabilistic independent component analysis for functional magnetic resonance imaging. *IEEE transactions on medical imaging* 23: 137-152

- Beijers L, Wardenaar KJ, van Loo HM, Schoevers RA (2019) Data-driven biological subtypes of depression: systematic review of biological approaches to depression subtyping. *Molecular psychiatry* 24: 888-900
- Belleau EL (2022) Parsing Heterogeneity in Mood Disorders: The Challenges of Modeling Stable Mood Disorder-Related Functional Connectomes. *Biological psychiatry Cognitive neuroscience and neuroimaging* 7: 7-9
- Belov V, Erwin-Grabner T, Aghajani M, Aleman A, Amod AR, Basgoze Z, Benedetti F, Besther B, Bülow R, Ching CRK *et al* (2024) Multi-site benchmark classification of major depressive disorder using machine learning on cortical and subcortical measures. *Scientific reports* 14: 1084
- Benjamini Y, Hochberg Y (2000) On the adaptive control of the false discovery rate in multiple testing with independent statistics. *Journal of educational Behavioral Statistics* 25: 60-83
- Berk M, Köhler-Forsberg O, Turner M, Penninx B, Wrobel A, Firth J, Loughman A, Reavley NJ, McGrath JJ, Momen NC *et al* (2023) Comorbidity between major depressive disorder and physical diseases: a comprehensive review of epidemiology, mechanisms and management. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 22: 366-387
- Berk M, Post R, Ratheesh A, Gliddon E, Singh A, Vieta E, Carvalho AF, Ashton MM, Berk L, Cotton SM *et al* (2017) Staging in bipolar disorder: from theoretical framework to clinical utility. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 16: 236-244
- Bernstein DP, Fink L, Handelsman L, Foote J (1998) Childhood trauma questionnaire. *Assessment of family violence: A handbook for researchers practitioners*
- Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, Stokes J, Handelsman L, Medrano M, Desmond D *et al* (2003) Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child abuse & neglect* 27: 169-190
- Bertollo AG, Puntel CF, da Silva BV, Martins M, Bagatini MD, Ignácio ZM (2025) Neurobiological Relationships Between Neurodevelopmental Disorders and Mood Disorders. *Brain sciences* 15

- Beurel E, Toups M, Nemeroff CB (2020) The Bidirectional Relationship of Depression and Inflammation: Double Trouble. *Neuron* 107: 234-256
- Boot EM, Mc van Leijssen E, Bergkamp MI, Kessels RPC, Norris DG, de Leeuw FE, Tuladhar AM (2020) Structural network efficiency predicts cognitive decline in cerebral small vessel disease. *NeuroImage Clinical* 27: 102325
- Bora E, Yücel M, Pantelis C (2010) Neurocognitive markers of psychosis in bipolar disorder: a meta-analytic study. *Journal of affective disorders* 127: 1-9
- Brown S, Rittenbach K, Cheung S, McKean G, MacMaster FP, Clement F (2019a) Current and Common Definitions of Treatment-Resistant Depression: Findings from a Systematic Review and Qualitative Interviews. *Canadian journal of psychiatry / Revue canadienne de psychiatrie* 64: 380-387
- Brown SSG, Rutland JW, Verma G, Feldman RE, Alper J, Schneider M, Delman BN, Murrough JM, Balchandani P (2019b) Structural MRI at 7T reveals amygdala nuclei and hippocampal subfield volumetric association with Major Depressive Disorder symptom severity. *Scientific reports* 9: 10166
- Brown SSG, Rutland JW, Verma G, Feldman RE, Schneider M, Delman BN, Murrough JM, Balchandani P (2020) Ultra-High-Resolution Imaging of Amygdala Subnuclei Structural Connectivity in Major Depressive Disorder. *Biological psychiatry Cognitive neuroscience and neuroimaging* 5: 184-193
- Bubb EJ, Metzler-Baddeley C, Aggleton JP (2018) The cingulum bundle: Anatomy, function, and dysfunction. *Neuroscience and biobehavioral reviews* 92: 104-127
- Buch AM, Liston C (2021) Dissecting diagnostic heterogeneity in depression by integrating neuroimaging and genetics. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 46: 156-175
- Buckman JEJ, Saunders R, Arundell LL, Oshinowo ID, Cohen ZD, O'Driscoll C, Barnett P, Stott J, Ambler G, Gilbody S *et al* (2022) Life events and treatment prognosis for depression: A systematic review and individual patient data meta-analysis. *Journal of affective disorders* 299: 298-308
- Bullock DN, Hayday EA, Grier MD, Tang W, Pestilli F, Heilbronner SR (2022) A taxonomy of the brain's white matter: twenty-one major tracts for the 21st century. *Cerebral cortex (New York, NY : 1991)* 32: 4524-4548

- Bycroft C, Freeman C, Petkova D, Band G, Elliott LT, Sharp K, Motyer A, Vukcevic D, Delaneau O, O'Connell J *et al* (2018) The UK Biobank resource with deep phenotyping and genomic data. *Nature* 562: 203-209
- Bzdok D, Meyer-Lindenberg A (2018) Machine Learning for Precision Psychiatry: Opportunities and Challenges. *Biological psychiatry Cognitive neuroscience and neuroimaging* 3: 223-230
- Cai H, Cai B, Zhang H, Sun W, Wang Y, Zhou S, Ye Z, Zhang Z, Liang J (2019) Major depression and small vessel stroke: a Mendelian randomization analysis. *Journal of neurology* 266: 2859-2866
- Cai N, Revez JA, Adams MJ, Andlauer TFM, Breen G, Byrne EM, Clarke TK, Forstner AJ, Grabe HJ, Hamilton SP *et al* (2020) Minimal phenotyping yields genome-wide association signals of low specificity for major depression. *Nature genetics* 52: 437-447
- Calafato MS, Thygesen JH, Ranlund S, Zartaloudi E, Cahn W, Crespo-Facorro B, Díez-Revuelta Á, Di Forti M, Hall MH, Iyegbe C *et al* (2018) Use of schizophrenia and bipolar disorder polygenic risk scores to identify psychotic disorders. *The British journal of psychiatry : the journal of mental science* 213: 535-541
- Caliński T, Harabasz J (1974) A dendrite method for cluster analysis. *Communications in Statistics-theory Methods* 3: 1-27
- Campello RJ, Moulavi D, Sander J, 2013. Density-based clustering based on hierarchical density estimates, Pacific-Asia conference on knowledge discovery and data mining. Springer, pp. 160-172.
- Cao Z, Ge L, Lu W, Zhao K, Chen Y, Sun Z, Qiu W, Yue X, Li Y, Qiu S (2024) Altered Subcortical Brain Volume and Cortical Thickness Related to Insulin Resistance in Type 2 Diabetes Mellitus. *Brain and behavior* 14: e70055
- Carballo JJ, Harkavy-Friedman J, Burke AK, Sher L, Baca-Garcia E, Sullivan GM, Grunebaum MF, Parsey RV, Mann JJ, Oquendo MA (2008) Family history of suicidal behavior and early traumatic experiences: additive effect on suicidality and course of bipolar illness? *Journal of affective disorders* 109: 57-63
- Cattarinussi G, Bellani M, Maggioni E, Sambataro F, Brambilla P, Delvecchio G (2022a) Resting-state functional connectivity and spontaneous brain activity in early-onset

- bipolar disorder: A review of functional Magnetic Resonance Imaging studies. *Journal of affective disorders* 311: 463-471
- Cattarinussi G, Delvecchio G, Sambataro F, Brambilla P (2022b) The effect of polygenic risk scores for major depressive disorder, bipolar disorder and schizophrenia on morphological brain measures: A systematic review of the evidence. *Journal of affective disorders* 310: 213-222
- Caviness VS, Jr., Meyer J, Makris N, Kennedy DN (1996) MRI-Based Topographic Parcellation of Human Neocortex: An Anatomically Specified Method with Estimate of Reliability. *Journal of cognitive neuroscience* 8: 566-587
- Chang K, Karchemskiy A, Barnea-Goraly N, Garrett A, Simeonova DI, Reiss A (2005) Reduced amygdalar gray matter volume in familial pediatric bipolar disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* 44: 565-573
- Chapman SB, Aslan S, Spence JS, Hart JJ, Jr., Bartz EK, Didehbani N, Keebler MW, Gardner CM, Strain JF, DeFina LF *et al* (2015) Neural mechanisms of brain plasticity with complex cognitive training in healthy seniors. *Cerebral cortex (New York, NY : 1991)* 25: 396-405
- Chen G, Hu X, Li L, Huang X, Lui S, Kuang W, Ai H, Bi F, Gu Z, Gong Q (2016) Disorganization of white matter architecture in major depressive disorder: a meta-analysis of diffusion tensor imaging with tract-based spatial statistics. *Scientific reports* 6: 21825
- Chen G, Wang J, Gong J, Qi Z, Fu S, Tang G, Chen P, Huang L, Wang Y (2022a) Functional and structural brain differences in bipolar disorder: a multimodal meta-analysis of neuroimaging studies. *Psychological medicine* 52: 2861-2873
- Chen Y, Li HT, Luo X, Li G, Ide JS, Li CR (2025) Polygenic risks for depression and neural responses to reward and punishment in young adults. *Biological psychiatry Cognitive neuroscience and neuroimaging*
- Chen ZS, Kulkarni PP, Galatzer-Levy IR, Bigio B, Nasca C, Zhang Y (2022b) Modern views of machine learning for precision psychiatry. *Patterns (New York, NY)* 3: 100602
- Cheng Y, Xu J, Yu H, Nie B, Li N, Luo C, Li H, Liu F, Bai Y, Shan B *et al* (2014) Delineation of early and later adult onset depression by diffusion tensor imaging. *PloS one* 9: e112307

- Chibaatar E, Watanabe K, Okamoto N, Orkhonselenge N, Natsuyama T, Hayakawa G, Ikenouchi A, Kakeda S, Yoshimura R (2023) Volumetric assessment of individual thalamic nuclei in patients with drug-naïve, first-episode major depressive disorder. *Frontiers in psychiatry* 14: 1151551
- Choi EY, Yeo BT, Buckner RL (2012) The organization of the human striatum estimated by intrinsic functional connectivity. *Journal of neurophysiology* 108: 2242-2263
- Choi RY, Coyner AS, Kalpathy-Cramer J, Chiang MF, Campbell JP (2020) Introduction to Machine Learning, Neural Networks, and Deep Learning. *Translational vision science & technology* 9: 14
- Ciechanowski PS, Katon WJ, Russo JE (2000) Depression and diabetes: impact of depressive symptoms on adherence, function, and costs. *Archives of internal medicine* 160: 3278-3285
- Cole MW, Reynolds JR, Power JD, Repovs G, Anticevic A, Braver TS (2013) Multi-task connectivity reveals flexible hubs for adaptive task control. *Nature neuroscience* 16: 1348-1355
- Coleman JRI, Peyrot WJ, Purves KL, Davis KAS, Rayner C, Choi SW, Hübel C, Gaspar HA, Kan C, Van der Auwera S *et al* (2020) Genome-wide gene-environment analyses of major depressive disorder and reported lifetime traumatic experiences in UK Biobank. *Molecular psychiatry* 25: 1430-1446
- Collins GS, Reitsma JB, Altman DG, Moons KG (2015) Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. *BMJ (Clinical research ed)* 350: g7594
- Colombo F, Calesella F, Bravi B, Fortaner-Uyà L, Monopoli C, Tassi E, Carminati M, Zanardi R, Bollettini I, Poletti S *et al* (2024) Multimodal brain-derived subtypes of Major depressive disorder differentiate patients for anergic symptoms, immune-inflammatory markers, history of childhood trauma and treatment-resistance. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology* 85: 45-57
- Conroy M, Sellors J, Effingham M, Littlejohns TJ, Boultonwood C, Gillions L, Sudlow CLM, Collins R, Allen NE (2019) The advantages of UK Biobank's open-access strategy for health research. *Journal of internal medicine* 286: 389-397

- CONVERGE Consortium (2015) Sparse whole-genome sequencing identifies two loci for major depressive disorder. *Nature* 523: 588-591
- Cooke EM, Connolly EJ, Boisvert DL, Hayes BE (2023) A Systematic Review of the Biological Correlates and Consequences of Childhood Maltreatment and Adverse Childhood Experiences. *Trauma, violence & abuse* 24: 156-173
- Coombes CE, Liu X, Abrams ZB, Coombes KR, Brock G (2021) Simulation-derived best practices for clustering clinical data. *Journal of biomedical informatics* 118: 103788
- Croall ID, Lohner V, Moynihan B, Khan U, Hassan A, O'Brien JT, Morris RG, Tozer DJ, Cambridge VC, Harkness K *et al* (2017) Using DTI to assess white matter microstructure in cerebral small vessel disease (SVD) in multicentre studies. *Clinical science (London, England : 1979)* 131: 1361-1373
- Cuijpers P, Miguel C, Ciharova M, Quero S, Plessen CY, Ebert D, Harrer M, van Straten A, Karyotaki E (2023) Psychological treatment of depression with other comorbid mental disorders: systematic review and meta-analysis. *Cognitive behaviour therapy* 52: 246-268
- Cunningham JP, Ghahramani Z (2015) Linear dimensionality reduction: Survey, insights, and generalizations. *The Journal of Machine Learning Research* 16: 2859-2900
- Curzytek K, Leśkiewicz M (2021) Targeting the CCL2-CCR2 axis in depressive disorders. *Pharmacological reports : PR* 73: 1052-1062
- Cusi AM, Nazarov A, Holshausen K, Macqueen GM, McKinnon MC (2012) Systematic review of the neural basis of social cognition in patients with mood disorders. *Journal of psychiatry & neuroscience : JPN* 37: 154-169
- Cuthbert BN (2022) Research Domain Criteria (RDoC): Progress and Potential. *Current directions in psychological science* 31: 107-114
- Cuthbert BN, Insel TR (2013) Toward the future of psychiatric diagnosis: the seven pillars of RDoC. *BMC medicine* 11: 126
- Dagani J, Signorini G, Nielssen O, Bani M, Pastore A, Girolamo G, Large M (2017) Meta-analysis of the Interval between the Onset and Management of Bipolar Disorder. *Canadian journal of psychiatry Revue canadienne de psychiatrie* 62: 247-258
- Dale AM, Fischl B, Sereno MI (1999) Cortical surface-based analysis. I. Segmentation and surface reconstruction. *NeuroImage* 9: 179-194

- Danielsdóttir HB, Aspelund T, Shen Q, Halldorsdottir T, Jakobsdóttir J, Song H, Lu D, Kuja-Halkola R, Larsson H, Fall K *et al* (2024) Adverse Childhood Experiences and Adult Mental Health Outcomes. *JAMA psychiatry* 81: 586-594
- Das S, Forer L, Schönherr S, Sidore C, Locke AE, Kwong A, Vrieze SI, Chew EY, Levy S, McGue M *et al* (2016) Next-generation genotype imputation service and methods. *Nature genetics* 48: 1284-1287
- Davies DL, Bouldin DW (2009) A cluster separation measure. *IEEE transactions on pattern analysis machine intelligence*: 224-227
- Davis K, Coleman JRI, Adams M, Allen N, Breen G, Cullen B, Dickens C, Fox E, Graham N, Holliday J *et al* (2020) Mental health in UK Biobank - development, implementation and results from an online questionnaire completed by 157 366 participants: a reanalysis. *BJPsych open* 6: e18
- de Groot M, Vernooij MW, Klein S, Ikram MA, Vos FM, Smith SM, Niessen WJ, Andersson JL (2013) Improving alignment in Tract-based spatial statistics: evaluation and optimization of image registration. *NeuroImage* 76: 400-411
- de Moor MH, van den Berg SM, Verweij KJ, Krueger RF, Luciano M, Arias Vasquez A, Matteson LK, Derringer J, Esko T, Amin N *et al* (2015) Meta-analysis of Genome-wide Association Studies for Neuroticism, and the Polygenic Association With Major Depressive Disorder. *JAMA psychiatry* 72: 642-650
- Dedeurwaerder S, Defrance M, Bizet M, Calonne E, Bontempi G, Fuks F (2014) A comprehensive overview of Infinium HumanMethylation450 data processing. *Briefings in bioinformatics* 15: 929-941
- Demontis D, Walters GB, Athanasiadis G, Walters R, Therrien K, Nielsen TT, Farajzadeh L, Voloudakis G, Bendl J, Zeng B *et al* (2023) Genome-wide analyses of ADHD identify 27 risk loci, refine the genetic architecture and implicate several cognitive domains. *Nature genetics* 55: 198-208
- DeRubeis RJ, Cohen ZD, Forand NR, Fournier JC, Gelfand LA, Lorenzo-Luaces L (2014) The Personalized Advantage Index: translating research on prediction into individualized treatment recommendations. A demonstration. *PloS one* 9: e83875
- Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, Buckner RL, Dale AM, Maguire RP, Hyman BT *et al* (2006) An automated labeling system for

- subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage* 31: 968-980
- Diaz AP, Fernandes BS, Quevedo J, Sanches M, Soares JC (2022) Treatment-resistant bipolar depression: concepts and challenges for novel interventions. *Revista brasileira de psiquiatria (Sao Paulo, Brazil : 1999)* 44: 178-186
- Dinga R, Schmaal L, Penninx B, van Tol MJ, Veltman DJ, van Velzen L, Mennes M, van der Wee NJA, Marquand AF (2019) Evaluating the evidence for biotypes of depression: Methodological replication and extension of Drysdale et al. (2017). *NeuroImage Clinical* 22: 101796
- Dodd S, Bauer M, Carvalho AF, Eyre H, Fava M, Kasper S, Kennedy SH, Khoo JP, Lopez Jaramillo C, Malhi GS *et al* (2021) A clinical approach to treatment resistance in depressed patients: What to do when the usual treatments don't work well enough? *The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry* 22: 483-494
- Dohm K, Redlich R, Zwitserlood P, Dannlowski U (2017) Trajectories of major depression disorders: A systematic review of longitudinal neuroimaging findings. *The Australian and New Zealand journal of psychiatry* 51: 441-454
- Douglas KM, Porter RJ (2009) Longitudinal assessment of neuropsychological function in major depression. *The Australian and New Zealand journal of psychiatry* 43: 1105-1117
- Douglas KM, Porter RJ, Young AH (2020) Cognition in mood disorders. *BJPsych open* 7: e16
- Drevets WC, Price JL, Furey ML (2008) Brain structural and functional abnormalities in mood disorders: implications for neurocircuitry models of depression. *Brain structure & function* 213: 93-118
- Drysdale AT, Grosenick L, Downar J, Dunlop K, Mansouri F, Meng Y, Fetcho RN, Zebley B, Oathes DJ, Etkin A *et al* (2017) Resting-state connectivity biomarkers define neurophysiological subtypes of depression. *Nature medicine* 23: 28-38
- Du Rietz E, Coleman J, Glanville K, Choi SW, O'Reilly PF, Kuntsi J (2018) Association of Polygenic Risk for Attention-Deficit/Hyperactivity Disorder With Co-occurring Traits and Disorders. *Biological psychiatry Cognitive neuroscience and neuroimaging* 3: 635-643

- Duman CH, Duman RS (2015) Spine synapse remodeling in the pathophysiology and treatment of depression. *Neuroscience letters* 601: 20-29
- Dusi N, Barlati S, Vita A, Brambilla P (2015) Brain Structural Effects of Antidepressant Treatment in Major Depression. *Current neuropharmacology* 13:458-465
- Dutt RK, Hannon K, Easley TO, Griffis JC, Zhang W, Bijsterbosch JD (2022) Mental health in the UK Biobank: A roadmap to self-report measures and neuroimaging correlates. *Human brain mapping* 43: 816-832
- Dwyer DB, Kalman JL, Budde M, Kambeitz J, Ruef A, Antonucci LA, Kambeitz-Ilankovic L, Hasan A, Kondofersky I, Anderson-Schmidt H *et al* (2020) An Investigation of Psychosis Subgroups With Prognostic Validation and Exploration of Genetic Underpinnings: The PsyCourse Study. *JAMA psychiatry* 77: 523-533
- Eckhardt CM, Madjarova SJ, Williams RJ, Ollivier M, Karlsson J, Pareek A, Nwachukwu BU (2023) Unsupervised machine learning methods and emerging applications in healthcare. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA* 31: 376-381
- ENIGMA, 2025. Structural imaging processing protocols.
- Etain B, Aas M, Andreassen OA, Lorentzen S, Dieset I, Gard S, Kahn JP, Bellivier F, Leboyer M, Melle I *et al* (2013) Childhood trauma is associated with severe clinical characteristics of bipolar disorders. *The Journal of clinical psychiatry* 74: 991-998
- Evans TE, O'Sullivan MJ, de Groot M, Niessen WJ, Hofman A, Krestin GP, van der Lugt A, Portegies ML, Koudstaal PJ, Bos D *et al* (2016) White Matter Microstructure Improves Stroke Risk Prediction in the General Population. *Stroke* 47: 2756-2762
- Fabbri C, Hagenaars SP, John C, Williams AT, Shrine N, Moles L, Hanscombe KB, Serretti A, Shepherd DJ, Free RC *et al* (2021) Genetic and clinical characteristics of treatment-resistant depression using primary care records in two UK cohorts. *Molecular psychiatry* 26: 3363-3373
- Fabbri C, Mutz J, Lewis CM, Serretti A (2022) Stratification of individuals with lifetime depression and low wellbeing in the UK Biobank. *Journal of affective disorders* 314: 281-292
- Fanelli G, Mota NR, Salas-Salvadó J, Bulló M, Fernandez-Aranda F, Camacho-Barcia L, Testa G, Jiménez-Murcia S, Bertaina-Anglade V, Franke B *et al* (2022) The link between cognition and somatic conditions related to insulin resistance in the UK

- Biobank study cohort: a systematic review. *Neuroscience and biobehavioral reviews* 143: 104927
- Fang Y, Fritsche LG, Mukherjee B, Sen S, Richmond-Rakerd LS (2022) Polygenic Liability to Depression Is Associated With Multiple Medical Conditions in the Electronic Health Record: Phenome-wide Association Study of 46,782 Individuals. *Biological psychiatry* 92: 923-931
- Fang Y, Qin T, Liu W, Ran L, Yang Y, Huang H, Pan D, Wang M (2020) Cerebral Small-Vessel Disease and Risk of Incidence of Depression: A Meta-Analysis of Longitudinal Cohort Studies. *Journal of the American Heart Association* 9: e016512
- Favre P, Pauling M, Stout J, Hozer F, Sarrazin S, Abé C, Alda M, Alloza C, Alonso-Lana S, Andreassen OA *et al* (2019) Widespread white matter microstructural abnormalities in bipolar disorder: evidence from mega- and meta-analyses across 3033 individuals. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 44: 2285-2293
- Filippini N, MacIntosh BJ, Hough MG, Goodwin GM, Frisoni GB, Smith SM, Matthews PM, Beckmann CF, Mackay CE (2009) Distinct patterns of brain activity in young carriers of the APOE-epsilon4 allele. *Proceedings of the National Academy of Sciences of the United States of America* 106: 7209-7214
- First MB, Williams JB, Karg RS, Spitzer RL (2015) Structured clinical interview for DSM-5 disorders. *Clinician Version*
- Firth J, Stubbs B, Teasdale SB, Ward PB, Veronese N, Shivappa N, Hebert JR, Berk M, Yung AR, Sarris J (2018) Diet as a hot topic in psychiatry: a population-scale study of nutritional intake and inflammatory potential in severe mental illness. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 17: 365-367
- Fornaro M, Carvalho AF, De Prisco M, Mondin AM, Billeci M, Selby P, Iasevoli F, Berk M, Castle DJ, de Bartolomeis A (2022) The prevalence, odds, predictors, and management of tobacco use disorder or nicotine dependence among people with severe mental illness: Systematic review and meta-analysis. *Neuroscience and biobehavioral reviews* 132: 289-303
- Fornito A, Zalesky A, Breakspear M (2015) The connectomics of brain disorders. *Nature reviews Neuroscience* 16: 159-172

- Fortin JP, Cullen N, Sheline YI, Taylor WD, Aselcioglu I, Cook PA, Adams P, Cooper C, Fava M, McGrath PJ *et al* (2018) Harmonization of cortical thickness measurements across scanners and sites. *NeuroImage* 167: 104-120
- Foti D, Carlson JM, Sauder CL, Proudfit GH (2014) Reward dysfunction in major depression: multimodal neuroimaging evidence for refining the melancholic phenotype. *NeuroImage* 101: 50-58
- Fountoulakis KN, Iacovides A, Gerasimou G, Fotiou F, Ioannidou C, Bascialla F, Grammaticos P, Kaprinis G (2004) The relationship of regional cerebral blood flow with subtypes of major depression. *Progress in neuro-psychopharmacology & biological psychiatry* 28: 537-546
- Fox J, Weisberg S (2018) *An R companion to applied regression*. Sage publications
- Fried EI (2017) The 52 symptoms of major depression: Lack of content overlap among seven common depression scales. *Journal of affective disorders* 208: 191-197
- Fried EI, Nesse RM (2015) Depression is not a consistent syndrome: An investigation of unique symptom patterns in the STAR*D study. *Journal of affective disorders* 172: 96-102
- Frodl T, Meisenzahl EM, Zetsche T, Born C, Jäger M, Groll C, Bottlender R, Leinsinger G, Möller HJ (2003) Larger amygdala volumes in first depressive episode as compared to recurrent major depression and healthy control subjects. *Biological psychiatry* 53: 338-344
- Fugger G, Waldhör T, Hinterbuchinger B, Pruckner N, König D, Gmeiner A, Vyssoki S, Vyssoki B, Fellingner M (2020) Pattern of inpatient care for depression: an analysis of 232,289 admissions. *BMC psychiatry* 20: 375
- Galimberti C, Bosi MF, Volontè M, Giordano F, Dell'Osso B, Viganò CA (2020) Duration of untreated illness and depression severity are associated with cognitive impairment in mood disorders. *International journal of psychiatry in clinical practice* 24: 227-235
- Gan G, Ma C, Wu J (2020) *Data clustering: theory, algorithms, and applications*. SIAM
- Gao CX, Dwyer D, Zhu Y, Smith CL, Du L, Filia KM, Bayer J, Menssink JM, Wang T, Bergmeir C *et al* (2023) An overview of clustering methods with guidelines for application in mental health research. *Psychiatry research* 327: 115265

- Gao S, Calhoun VD, Sui J (2018) Machine learning in major depression: From classification to treatment outcome prediction. *CNS neuroscience & therapeutics* 24: 1037-1052
- GBD 2019 Mental Disorders Collaborators (2022) Global, regional, and national burden of 12 mental disorders in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *The lancet Psychiatry* 9: 137-150
- Gerlach AR, Karim HT, Peciña M, Ajilore O, Taylor WD, Butters MA, Andreescu C (2022) MRI predictors of pharmacotherapy response in major depressive disorder. *NeuroImage Clinical* 36: 103157
- Gibbons RD, Dorus E, Ostrow DG, Pandey GN, Davis JM, Levy DL (1984) Mixture distributions in psychiatric research. *Biological psychiatry* 19: 935-961
- Glaesmer H, Schulz A, Häuser W, Freyberger HJ, Brähler E, Grabe HJ (2013) [The childhood trauma screener (CTS) - development and validation of cut-off-scores for classificatory diagnostics]. *Psychiatrische Praxis* 40: 220-226
- Glasser MF, Sotiropoulos SN, Wilson JA, Coalson TS, Fischl B, Andersson JL, Xu J, Jbabdi S, Webster M, Polimeni JR *et al* (2013) The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* 80: 105-124
- Godlewska BR, Browning M, Norbury R, Igoumenou A, Cowen PJ, Harmer CJ (2018) Predicting Treatment Response in Depression: The Role of Anterior Cingulate Cortex. *The international journal of neuropsychopharmacology* 21: 988-996
- Godlewska BR, Harmer CJ (2021) Cognitive neuropsychological theory of antidepressant action: a modern-day approach to depression and its treatment. *Psychopharmacology* 238: 1265-1278
- Goldberg DJWP (2011) The heterogeneity of “major depression”. 10: 226
- Gong J, Wang J, Chen P, Qi Z, Luo Z, Wang J, Huang L, Wang Y (2021) Large-scale network abnormality in bipolar disorder: A multimodal meta-analysis of resting-state functional and structural magnetic resonance imaging studies. *Journal of affective disorders* 292: 9-20
- Gong Q, Wang W, Nie Z, Ma S, Zhou E, Deng Z, Xie XH, Lyu H, Chen MM, Kang L *et al* (2025) Correlation between polygenic risk scores of depression and cortical morphology networks. *Journal of psychiatry & neuroscience : JPN* 50: E21-e30

- Gonzalez JS, Peyrot M, McCarl LA, Collins EM, Serpa L, Mimiaga MJ, Safren SA (2008) Depression and diabetes treatment nonadherence: a meta-analysis. *Diabetes care* 31: 2398-2403
- Gordovez FJA, McMahon FJ (2020) The genetics of bipolar disorder. *Molecular psychiatry* 25: 544-559
- Graham EA, Deschênes SS, Khalil MN, Danna S, Fillion KB, Schmitz N (2020) Measures of depression and risk of type 2 diabetes: A systematic review and meta-analysis. *Journal of affective disorders* 265: 224-232
- Graham SE, Clarke SL, Wu KH, Kanoni S, Zajac GJM, Ramdas S, Surakka I, Ntalla I, Vedantam S, Winkler TW *et al* (2021) The power of genetic diversity in genome-wide association studies of lipids. *Nature* 600: 675-679
- Grande I, Berk M, Birmaher B, Vieta E (2016) Bipolar disorder. *The Lancet* 387: 1561-1572
- Green EK, Rees E, Walters JT, Smith KG, Forty L, Grozeva D, Moran JL, Sklar P, Ripke S, Chambert KD *et al* (2016) Copy number variation in bipolar disorder. *Molecular psychiatry* 21: 89-93
- Greve DN, Fischl B (2009) Accurate and robust brain image alignment using boundary-based registration. *NeuroImage* 48: 63-72
- Griffanti L, Salimi-Khorshidi G, Beckmann CF, Auerbach EJ, Douaud G, Sexton CE, Zsoldos E, Ebmeier KP, Filippini N, Mackay CE *et al* (2014) ICA-based artefact removal and accelerated fMRI acquisition for improved resting state network imaging. *NeuroImage* 95: 232-247
- Grigoriu-Serbanescu M, Giaroli G, Thygesen JH, Shenyan O, Bigdeli TB, Bass NJ, Diaconu CC, Neagu AI, Forstner AJ, Degenhardt F *et al* (2020) Predictive power of the ADHD GWAS 2019 polygenic risk scores in independent samples of bipolar patients with childhood ADHD. *Journal of affective disorders* 265: 651-659
- Groenewold NA, Opmeer EM, de Jonge P, Aleman A, Costafreda SG (2013) Emotional valence modulates brain functional abnormalities in depression: evidence from a meta-analysis of fMRI studies. *Neuroscience and biobehavioral reviews* 37: 152-163
- Gronewold J, Duman EE, Engel M, Engels M, Siegrist J, Erbel R, Jöckel KH, Hermann DM (2022) Association between life events and later depression in the population-

- based Heinz Nixdorf Recall study-The role of sex and optimism. *PloS one* 17: e0271716
- Grosenick L, Shi TC, Gunning FM, Dubin MJ, Downar J, Liston C (2019) Functional and Optogenetic Approaches to Discovering Stable Subtype-Specific Circuit Mechanisms in Depression. *Biological psychiatry Cognitive neuroscience and neuroimaging* 4: 554-566
- Grove J, Ripke S, Als TD, Mattheisen M, Walters RK, Won H, Pallesen J, Agerbo E, Andreassen OA, Anney R *et al* (2019) Identification of common genetic risk variants for autism spectrum disorder. *Nature genetics* 51: 431-444
- Hafeman DM, Uher R, Merranko J, Zwicker A, Goldstein B, Goldstein TR, Axelson D, Monk K, Sakolsky D, Iyengar S *et al* (2025) Person-level contributions of bipolar polygenic risk score to the prediction of new-onset bipolar disorder in at-risk offspring. *Journal of affective disorders* 368: 359-365
- Hajek T, Kopecek M, Kozeny J, Gunde E, Alda M, Höschl C (2009) Amygdala volumes in mood disorders--meta-analysis of magnetic resonance volumetry studies. *Journal of affective disorders* 115: 395-410
- Halkidi M, Batistakis Y, Vazirgiannis M (2001) On clustering validation techniques. *Journal of intelligent information systems* 17: 107-145
- Halldorsdottir T, Piechaczek C, Soares de Matos AP, Czamara D, Pehl V, Wagenbuechler P, Feldmann L, Quickenstedt-Reinhardt P, Allgaier AK, Freisleder FJ *et al* (2019) Polygenic Risk: Predicting Depression Outcomes in Clinical and Epidemiological Cohorts of Youths. *The American journal of psychiatry* 176: 615-625
- Hamilton JP, Etkin A, Furman DJ, Lemus MG, Johnson RF, Gotlib IH (2012) Functional neuroimaging of major depressive disorder: a meta-analysis and new integration of base line activation and neural response data. *The American journal of psychiatry* 169: 693-703
- Hamilton M (1960) A rating scale for depression. *Journal of neurology, neurosurgery, psychiatry* 23: 56
- Harder A, Nguyen TD, Pasma JA, Mosing MA, Hägg S, Lu Y (2022) Genetics of age-at-onset in major depression. *Translational psychiatry* 12: 124

- Hariri AR, Tessitore A, Mattay VS, Fera F, Weinberger DR (2002) The amygdala response to emotional stimuli: a comparison of faces and scenes. *NeuroImage* 17: 317-323
- Harmer CJ, Duman RS, Cowen PJ (2017) How do antidepressants work? New perspectives for refining future treatment approaches. *The Lancet Psychiatry* 4:409-418
- Hart H, Rubia K (2012) Neuroimaging of child abuse: a critical review. *Frontiers in human neuroscience* 6: 52
- Hasler G (2010) Pathophysiology of depression: do we have any solid evidence of interest to clinicians? *World psychiatry : official journal of the World Psychiatric Association (WPA)* 9: 155-161
- Hayes JF, Miles J, Walters K, King M, Osborn DP (2015) A systematic review and meta-analysis of premature mortality in bipolar affective disorder. *Acta psychiatrica Scandinavica* 131: 417-425
- Heany SJ, Groenewold NA, Uhlmann A, Dalvie S, Stein DJ, Brooks SJ (2018) The neural correlates of Childhood Trauma Questionnaire scores in adults: A meta-analysis and review of functional magnetic resonance imaging studies. *Development and psychopathology* 30: 1475-1485
- Heim C, Shugart M, Craighead WE, Nemeroff CB (2010) Neurobiological and psychiatric consequences of child abuse and neglect. *Developmental psychobiology* 52: 671-690
- Herman JP, McKlveen JM, Ghosal S, Kopp B, Wulsin A, Makinson R, Scheimann J, Myers B (2016) Regulation of the Hypothalamic-Pituitary-Adrenocortical Stress Response. *Comprehensive Physiology* 6: 603-621
- Herrman H, Patel V, Kieling C, Berk M, Buchweitz C, Cuijpers P, Furukawa TA, Kessler RC, Kohrt BA, Maj M *et al* (2022) Time for united action on depression: a Lancet-World Psychiatric Association Commission. *Lancet (London, England)* 399: 957-1022
- Hibar DP, Westlye LT, Doan NT, Jahanshad N, Cheung JW, Ching CRK, Versace A, Bilderbeck AC, Uhlmann A, Mwangi B *et al* (2018) Cortical abnormalities in bipolar disorder: an MRI analysis of 6503 individuals from the ENIGMA Bipolar Disorder Working Group. *Molecular psychiatry* 23: 932-942

- Hibar DP, Westlye LT, van Erp TG, Rasmussen J, Leonardo CD, Faskowitz J, Haukvik UK, Hartberg CB, Doan NT, Agartz I *et al* (2016) Subcortical volumetric abnormalities in bipolar disorder. *Molecular psychiatry* 21: 1710-1716
- Holmes TH, Rahe RH (1967) The Social Readjustment Rating Scale. *Journal of psychosomatic research* 11: 213-218
- Honey CJ, Sporns O, Cammoun L, Gigandet X, Thiran JP, Meuli R, Hagmann P (2009) Predicting human resting-state functional connectivity from structural connectivity. *Proceedings of the National Academy of Sciences of the United States of America* 106: 2035-2040
- Hoogenboom WS, Marder TJ, Flores VL, Huisman S, Eaton HP, Schneiderman JS, Bolo NR, Simonson DC, Jacobson AM, Kubicki M *et al* (2014) Cerebral white matter integrity and resting-state functional connectivity in middle-aged patients with type 2 diabetes. *Diabetes* 63: 728-738
- Howard DM, Adams MJ, Clarke TK, Hafferty JD, Gibson J, Shirali M, Coleman JRI, Hagenaars SP, Ward J, Wigmore EM *et al* (2019) Genome-wide meta-analysis of depression identifies 102 independent variants and highlights the importance of the prefrontal brain regions. *Nature neuroscience* 22: 343-352
- Howard DM, Folkersen L, Coleman JRI, Adams MJ, Glanville K, Werge T, Hagenaars SP, Han B, Porteous D, Campbell A *et al* (2020) Genetic stratification of depression in UK Biobank. *Translational psychiatry* 10: 163
- Huang H, Liu Y, Yuan M, Marron JS (2015) Statistical Significance of Clustering using Soft Thresholding. *Journal of computational and graphical statistics : a joint publication of American Statistical Association, Institute of Mathematical Statistics, Interface Foundation of North America* 24: 975-993
- Huang L, Zhang Q, Tang T, Yang M, Chen C, Tao J, Liang S (2021) Abnormalities of Brain White Matter in Type 2 Diabetes Mellitus: A Meta-Analysis of Diffusion Tensor Imaging. *Frontiers in aging neuroscience* 13: 693890
- Huys QJ, Maia TV, Frank MJ (2016) Computational psychiatry as a bridge from neuroscience to clinical applications. *Nature neuroscience* 19: 404-413
- Hyvärinen A (1999) Fast and robust fixed-point algorithms for independent component analysis. *IEEE transactions on neural networks* 10: 626-634

- Ichikawa N, Lisi G, Yahata N, Okada G, Takamura M, Hashimoto RI, Yamada T, Yamada M, Suhara T, Moriguchi S *et al* (2020) Primary functional brain connections associated with melancholic major depressive disorder and modulation by antidepressants. *Scientific reports* 10: 3542
- Illumina, 2025a. Infinium PsychArray-24 Kit.
- Illumina, 2025b. Infinium Global Screening Array-24 Kit.
- Illumina, 2025c. Consortia Boosters to Flagship Arrays.
- Insel T (2014) The NIMH Research Domain Criteria (RDoC) Project: precision medicine for psychiatry. *The American journal of psychiatry* 171: 395-397
- Insel T, Cuthbert B, Garvey M, Heinssen R, Pine DS, Quinn K, Sanislow C, Wang P (2010) Research domain criteria (RDoC): toward a new classification framework for research on mental disorders. *The American journal of psychiatry* 167: 748-751
- IOCDF-GC and OCGAS (2018) Revealing the complex genetic architecture of obsessive-compulsive disorder using meta-analysis. *Molecular psychiatry* 23: 1181-1188
- Ionescu DF, Rosenbaum JF, Alpert JE (2015) Pharmacological approaches to the challenge of treatment-resistant depression. *Dialogues in clinical neuroscience* 17: 111-126
- Jain AK (2010) Data clustering: 50 years beyond K-means. *Pattern recognition letters* 31: 651-666
- Jajuga K, Walesiak M, 2000. Standardisation of data set under different measurement scales, Classification and Information Processing at the Turn of the Millennium: Proceedings of the 23rd Annual Conference of the Gesellschaft für Klassifikation eV, University of Bielefeld, March 10–12, 1999. Springer, pp. 105-112.
- Janiri D, Sani G, De Rossi P, Piras F, Banaj N, Ciullo V, Simonetti A, Arciniegas DB, Spalletta G (2019) Hippocampal subfield volumes and childhood trauma in bipolar disorders. *Journal of affective disorders* 253: 35-43
- Javaheripour N, Li M, Chand T, Krug A, Kircher T, Dannlowski U, Nenadić I, Hamilton JP, Sacchet MD, Gotlib IH *et al* (2021) Altered resting-state functional connectome in major depressive disorder: a mega-analysis from the PsyMRI consortium. *Translational psychiatry* 11: 511

- Jenkinson M, Bannister P, Brady M, Smith SM (2002) Improved optimization for the robust and accurate linear registration and motion correction of brain images. *NeuroImage* 17: 825-841
- Jenkinson M, Beckmann CF, Behrens TE, Woolrich MW, Smith SM (2012) FSL. *NeuroImage* 62: 782-790
- Jenkinson M, Smith SM (2001) A global optimisation method for robust affine registration of brain images. *Medical image analysis* 5: 143-156
- Jensen TM, Bernard D, Lanier P (2024) Conceptualizing adverse childhood experiences as a latent factor: Tests of measurement invariance across five racial and ethnic groups. *Child development* 95: e170-e185
- Jermey BS, Glanville KP, Coleman JRI, Lewis CM, Vassos E (2021) Exploring the genetic heterogeneity in major depression across diagnostic criteria. *Molecular psychiatry* 26: 7337-7345
- Jiang R, Calhoun VD, Noble S, Sui J, Liang Q, Qi S, Scheinost D (2023a) A functional connectome signature of blood pressure in >30 000 participants from the UK biobank. *Cardiovascular research* 119: 1427-1440
- Jiang X, Zai CC, Kennedy KG, Zou Y, Nikolova YS, Felsky D, Young LT, MacIntosh BJ, Goldstein BI (2023b) Association of polygenic risk for bipolar disorder with grey matter structure and white matter integrity in youth. *Translational psychiatry* 13: 322
- Jiang X, Zai CC, Merranko J, Young LT, Birmaher B, Goldstein BI (2025) Psychiatric Polygenic Risk Scores and Week-by-Week Symptomatic Status in Youth with Bipolar Disorder: An Exploratory Study. *Journal of child and adolescent psychopharmacology* 35: 269-276
- Johnson EC, Demontis D, Thorgeirsson TE, Walters RK, Polimanti R, Hatoum AS, Sanchez-Roige S, Paul SE, Wendt FR, Clarke TK *et al* (2020) A large-scale genome-wide association study meta-analysis of cannabis use disorder. *The lancet Psychiatry* 7: 1032-1045
- Johnson SL (2005) Life events in bipolar disorder: towards more specific models. *Clinical psychology review* 25: 1008-1027
- Johnson SL, Roberts JE (1995) Life events and bipolar disorder: implications from biological theories. *Psychological bulletin* 117: 434-449

- Jolliffe I (2022) A 50-year personal journey through time with principal component analysis. *Journal of Multivariate Analysis* 188: 104820
- Joslyn C, Hawes DJ, Hunt C, Mitchell PB (2016) Is age of onset associated with severity, prognosis, and clinical features in bipolar disorder? A meta-analytic review. *Bipolar disorders* 18: 389-403
- Juruena MF, Bocharova M, Agustini B, Young AH (2018) Atypical depression and non-atypical depression: Is HPA axis function a biomarker? A systematic review. *Journal of affective disorders* 233: 45-67
- Juruena MF, Eror F, Cleare AJ, Young AH (2020) The Role of Early Life Stress in HPA Axis and Anxiety. *Advances in experimental medicine and biology* 1191: 141-153
- Kaiser HF (1960) The application of electronic computers to factor analysis. *Educational psychological measurement* 20: 141-151
- Kaiser RH, Andrews-Hanna JR, Spielberg JM, Warren SL, Sutton BP, Miller GA, Heller W, Banich MT (2015a) Distracted and down: neural mechanisms of affective interference in subclinical depression. *Social cognitive and affective neuroscience* 10: 654-663
- Kaiser RH, Andrews-Hanna JR, Wager TD, Pizzagalli DA (2015b) Large-Scale Network Dysfunction in Major Depressive Disorder: A Meta-analysis of Resting-State Functional Connectivity. *JAMA psychiatry* 72: 603-611
- Kalman JL, Olde Loohuis LM, Vreeker A, McQuillin A, Stahl EA, Ruderfer D, Grigoriu-Serbanescu M, Panagiotaropoulou G, Ripke S, Bigdeli TB *et al* (2021) Characterisation of age and polarity at onset in bipolar disorder. *The British journal of psychiatry : the journal of mental science* 219: 659-669
- Kapur S, Phillips AG, Insel TR (2012) Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it? *Molecular psychiatry* 17: 1174-1179
- Kassambara A (2023) *rstatix: Pipe-Friendly Framework for Basic Statistical Tests*
- Kaufman J, Plotsky PM, Nemeroff CB, Charney DS (2000) Effects of early adverse experiences on brain structure and function: clinical implications. *Biological psychiatry* 48: 778-790
- Keefe RS, Goldberg TE, Harvey PD, Gold JM, Poe MP, Coughenour L (2004) The Brief Assessment of Cognition in Schizophrenia: reliability, sensitivity, and comparison with a standard neurocognitive battery. *Schizophrenia research* 68: 283-297

- Kelly S, Jahanshad N, Zalesky A, Kochunov P, Agartz I, Alloza C, Andreassen OA, Arango C, Banaj N, Bouix S *et al* (2018) Widespread white matter microstructural differences in schizophrenia across 4322 individuals: results from the ENIGMA Schizophrenia DTI Working Group. *Molecular psychiatry* 23: 1261-1269
- Kendall KM, Van Assche E, Andlauer TFM, Choi KW, Luykx JJ, Schulte EC, Lu Y (2021) The genetic basis of major depression. *Psychological medicine* 51: 2217-2230
- Kendler KS, Eaves LJ, Walters EE, Neale MC, Heath AC, Kessler RC (1996) The identification and validation of distinct depressive syndromes in a population-based sample of female twins. *Archives of general psychiatry* 53: 391-399
- Kendler KS, Karkowski LM, Prescott CA (1999) Causal relationship between stressful life events and the onset of major depression. *The American journal of psychiatry* 156: 837-841
- Kendler KS, Ohlsson H, Lichtenstein P, Sundquist J, Sundquist K (2018) The Genetic Epidemiology of Treated Major Depression in Sweden. *The American journal of psychiatry* 175: 1137-1144
- Kessler RC, Chiu WT, Demler O, Merikangas KR, Walters EE (2005) Prevalence, severity, and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of general psychiatry* 62: 617-627
- Kessler RC, van Loo HM, Wardenaar KJ, Bossarte RM, Brenner LA, Ebert DD, de Jonge P, Nierenberg AA, Rosellini AJ, Sampson NA *et al* (2017) Using patient self-reports to study heterogeneity of treatment effects in major depressive disorder. *Epidemiology and psychiatric sciences* 26: 22-36
- Kim H, Han KM, Choi KW, Tae WS, Kang W, Kang Y, Kim A, Ham BJ (2021) Volumetric alterations in subregions of the amygdala in adults with major depressive disorder. *Journal of affective disorders* 295: 108-115
- Kleemann R, Bucala R (2010) Macrophage migration inhibitory factor: critical role in obesity, insulin resistance, and associated comorbidities. *Mediators of inflammation* 2010: 610479
- Kleinman A, Caetano SC, Brentani H, Rocca CC, dos Santos B, Andrade ER, Zeni CP, Tramontina S, Rohde LA, Lafer B (2015) Attention-based classification pattern, a research domain criteria framework, in youths with bipolar disorder and attention-

- deficit/hyperactivity disorder. *The Australian and New Zealand journal of psychiatry* 49: 255-265
- Klem H, Hocky GM, McCullagh M (2022) Size-and-Shape Space Gaussian Mixture Models for Structural Clustering of Molecular Dynamics Trajectories. *Journal of chemical theory and computation* 18: 3218-3230
- Köhler CA, Freitas TH, Maes M, de Andrade NQ, Liu CS, Fernandes BS, Stubbs B, Solmi M, Veronese N, Herrmann N *et al* (2017) Peripheral cytokine and chemokine alterations in depression: a meta-analysis of 82 studies. *Acta psychiatrica Scandinavica* 135: 373-387
- Konieczny MJ, Omarov M, Zhang L, Malik R, Richardson TG, Baumeister SE, Bernhagen J, Dichgans M, Georgakis MK (2025) The genomic architecture of circulating cytokine levels points to drug targets for immune-related diseases. *Communications biology* 8: 34
- Koolschijn PC, van Haren NE, Lensvelt-Mulders GJ, Hulshoff Pol HE, Kahn RS (2009) Brain volume abnormalities in major depressive disorder: a meta-analysis of magnetic resonance imaging studies. *Human brain mapping* 30: 3719-3735
- Kotoula V, Evans JW, Punturieri C, Johnson SC, Zarate CA, Jr. (2023) Functional MRI markers for treatment-resistant depression: Insights and challenges. *Progress in brain research* 278: 117-148
- Kotov R, Krueger RF, Watson D, Achenbach TM, Althoff RR, Bagby RM, Brown TA, Carpenter WT, Caspi A, Clark LA *et al* (2017) The Hierarchical Taxonomy of Psychopathology (HiTOP): A dimensional alternative to traditional nosologies. *Journal of abnormal psychology* 126: 454-477
- Kozel FA, Trivedi MH, Wisniewski SR, Miyahara S, Husain MM, Fava M, Lebowitz B, Zisook S, Rush AJ (2008) Treatment outcomes for older depressed patients with earlier versus late onset of first depressive episode: a Sequenced Treatment Alternatives to Relieve Depression (STAR*D) report. *The American journal of geriatric psychiatry : official journal of the American Association for Geriatric Psychiatry* 16: 58-64
- Krantz MF, Hjorthøj C, Ellersgaard D, Hemager N, Christiani C, Spang KS, Burton BK, Gregersen M, Søndergaard A, Greve A *et al* (2023) Examining selection bias in a population-based cohort study of 522 children with familial high risk of

- schizophrenia or bipolar disorder, and controls: The Danish High Risk and Resilience Study VIA 7. *Social psychiatry and psychiatric epidemiology* 58: 113-140
- Kroenke K, Spitzer RL, Williams JB (2001) The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine* 16: 606-613
- Kullmann S, Kleinridders A, Small DM, Fritsche A, Häring HU, Preissl H, Heni M (2020) Central nervous pathways of insulin action in the control of metabolism and food intake. *The lancet Diabetes & endocrinology* 8: 524-534
- Kurki MI, Karjalainen J, Palta P, Sipilä TP, Kristiansson K, Donner KM, Reeve MP, Laivuori H, Aavikko M, Kaunisto MA *et al* (2023) FinnGen provides genetic insights from a well-phenotyped isolated population. *Nature* 613: 508-518
- Kustubayeva A, Eliassen J, Matthews G, Nelson E (2023) FMRI study of implicit emotional face processing in patients with MDD with melancholic subtype. *Frontiers in human neuroscience* 17: 1029789
- Lai CH (2013) Gray matter volume in major depressive disorder: a meta-analysis of voxel-based morphometry studies. *Psychiatry research* 211: 37-46
- Lamers F, Burstein M, He JP, Avenevoli S, Angst J, Merikangas KR (2012) Structure of major depressive disorder in adolescents and adults in the US general population. *The British journal of psychiatry : the journal of mental science* 201: 143-150
- Lamers F, de Jonge P, Nolen WA, Smit JH, Zitman FG, Beekman AT, Penninx BW (2010) Identifying depressive subtypes in a large cohort study: results from the Netherlands Study of Depression and Anxiety (NESDA). *The Journal of clinical psychiatry* 71: 1582-1589
- Latalova K, Prasko J, Diveky T, Velartova H (2011) Cognitive impairment in bipolar disorder. *Biomedical papers of the Medical Faculty of the University Palacky, Olomouc, Czechoslovakia* 155: 19-26
- Lawrence AJ, Chung AW, Morris RG, Markus HS, Barrick TR (2014) Structural network efficiency is associated with cognitive impairment in small-vessel disease. *Neurology* 83: 304-311
- Léda-Rêgo G, Studart-Bottó P, Abbade P, Rabelo-Da-Ponte FD, Casqueiro JS, Sarmiento S, Dallalana C, Troesch M, Prates S, Miranda-Scippa Â (2024) Lifetime prevalence of psychiatric comorbidities in patients with bipolar disorder: A systematic review and meta-analysis. *Psychiatry research* 337: 115953

- Lee CH, Yoon HJ (2017) Medical big data: promise and challenges. *Kidney research and clinical practice* 36: 3-11
- Lee EE, Torous J, De Choudhury M, Depp CA, Graham SA, Kim HC, Paulus MP, Krystal JH, Jeste DV (2021) Artificial Intelligence for Mental Health Care: Clinical Applications, Barriers, Facilitators, and Artificial Wisdom. *Biological psychiatry Cognitive neuroscience and neuroimaging* 6: 856-864
- Lee JJ, Wedow R, Okbay A, Kong E, Maghzian O, Zacher M, Nguyen-Viet TA, Bowers P, Sidorenko J, Karlsson Linnér R *et al* (2018) Gene discovery and polygenic prediction from a genome-wide association study of educational attainment in 1.1 million individuals. *Nature genetics* 50: 1112-1121
- Lee RS, Sawa A (2014) Environmental stressors and epigenetic control of the hypothalamic-pituitary-adrenal axis. *Neuroendocrinology* 100: 278-287
- Lee S, Abecasis GR, Boehnke M, Lin X (2014) Rare-variant association analysis: study designs and statistical tests. *American journal of human genetics* 95: 5-23
- Lee TY, Jo HJ, Koike S, Raballo A (2022) Editorial: Biotyping in Psychiatry. *Frontiers in psychiatry* 13: 844206
- Legemaat AM, Semkovska M, Brouwer M, Geurtsen GJ, Burger H, Denys D, Bockting CL (2021) Effectiveness of cognitive remediation in depression: a meta-analysis. *Psychological medicine* 52: 1-16
- Leighton SP, Nerurkar L, Krishnadas R, Johnman C, Graham GJ, Cavanagh J (2018) Chemokines in depression in health and in inflammatory illness: a systematic review and meta-analysis. *Molecular psychiatry* 23: 48-58
- Lever J, Krzywinski M, Altman N (2017) Points of significance: Principal component analysis. *Nature methods* 14: 641-643
- Levinson DF, Mostafavi S, Milaneschi Y, Rivera M, Ripke S, Wray NR, Sullivan PF (2014) Genetic studies of major depressive disorder: why are there no genome-wide association study findings and what can we do about it? *Biological psychiatry* 76: 510-512
- Lewandowski KE, Sperry SH, Cohen BM, Ongür D (2014) Cognitive variability in psychotic disorders: a cross-diagnostic cluster analysis. *Psychological medicine* 44: 3239-3248

- Lewis CM, Vassos E (2020) Polygenic risk scores: from research tools to clinical instruments. *Genome medicine* 12: 44
- Lex C, Bätzner E, Meyer TD (2017) Does stress play a significant role in bipolar disorder? A meta-analysis. *Journal of affective disorders* 208: 298-308
- Li GH, Cheung CL, Chung AK, Cheung BM, Wong IC, Fok MLY, Au PC, Sham PC (2022) Evaluation of bi-directional causal association between depression and cardiovascular diseases: a Mendelian randomization study. *Psychological medicine* 52: 1765-1776
- Li Q, Zhao Y, Chen Z, Long J, Dai J, Huang X, Lui S, Radua J, Vieta E, Kemp GJ *et al* (2020) Meta-analysis of cortical thickness abnormalities in medication-free patients with major depressive disorder. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 45: 703-712
- Liang S, Deng W, Li X, Greenshaw AJ, Wang Q, Li M, Ma X, Bai TJ, Bo QJ, Cao J *et al* (2020) Biotypes of major depressive disorder: Neuroimaging evidence from resting-state default mode network patterns. *NeuroImage Clinical* 28: 102514
- Liao H, Wu Y, Chen L, Chen W (2017) Cluster-based visual abstraction for multivariate scatterplots. *IEEE transactions on visualization computer graphics* 24: 2531-2545
- Liao Y, Huang X, Wu Q, Yang C, Kuang W, Du M, Lui S, Yue Q, Chan RC, Kemp GJ *et al* (2013) Is depression a disconnection syndrome? Meta-analysis of diffusion tensor imaging studies in patients with MDD. *Journal of psychiatry & neuroscience : JPN* 38: 49-56
- Ligthart S, Vaez A, Võsa U, Stathopoulou MG, de Vries PS, Prins BP, Van der Most PJ, Tanaka T, Naderi E, Rose LM *et al* (2018) Genome Analyses of >200,000 Individuals Identify 58 Loci for Chronic Inflammation and Highlight Pathways that Link Inflammation and Complex Disorders. *American journal of human genetics* 103: 691-706
- Lin EH, Katon W, Von Korff M, Rutter C, Simon GE, Oliver M, Ciechanowski P, Ludman EJ, Bush T, Young B (2004) Relationship of depression and diabetes self-care, medication adherence, and preventive care. *Diabetes care* 27: 2154-2160
- Lin Y, Lin P, Zeng G, Wu S, Chen R, Xiao Y, Chen H (2025) The impact of depression and anxiety on the correlation between somatic symptom disorder and subjective

- cognitive decline in the Chinese elderly population: an exploration by simple, serial, and moderated mediation models. *Frontiers in psychology* 16: 1545325
- Linthicum KP, Schafer KM, Ribeiro JD (2019) Machine learning in suicide science: Applications and ethics. *Behavioral sciences & the law* 37: 214-222
- Lippitt W, Carlson NE, Arbet J, Fingerlin TE, Maier LA, Kechris K (2024) Limitations of Clustering with PCA and Correlated Noise. *Journal of statistical computation and simulation* 94: 2291-2319
- Liu Y, Hayes DN, Nobel A, Marron JS (2008) Statistical significance of clustering for high-dimension, low-sample size data. *Journal of the American Statistical Association* 103: 1281-1293
- Liu Y, Leong ATL, Zhao Y, Xiao L, Mak HKF, Tsang ACO, Lau GKK, Leung GKK, Wu EX (2021) A low-cost and shielding-free ultra-low-field brain MRI scanner. *Nature communications* 12: 7238
- Liu Y, Li Z, Xiong H, Gao X, Wu J, Wu S (2013) Understanding and enhancement of internal clustering validation measures. *IEEE transactions on cybernetics* 43: 982-994
- Locke AE, Kahali B, Berndt SI, Justice AE, Pers TH, Day FR, Powell C, Vedantam S, Buchkovich ML, Yang J *et al* (2015) Genetic studies of body mass index yield new insights for obesity biology. *Nature* 518: 197-206
- López-Jaramillo C, Vargas C, Díaz-Zuluaga AM, Palacio JD, Castrillón G, Bearden C, Vieta E (2017) Increased hippocampal, thalamus and amygdala volume in long-term lithium-treated bipolar I disorder patients compared with unmedicated patients and healthy subjects. *Bipolar disorders* 19: 41-49
- Lorenzetti V, Allen NB, Fornito A, Yücel M (2009) Structural brain abnormalities in major depressive disorder: a selective review of recent MRI studies. *Journal of affective disorders* 117: 1-17
- Lorenzo-Luaces L, Buss JF, Fried EI (2021) Heterogeneity in major depression and its melancholic and atypical specifiers: a secondary analysis of STAR*D. *BMC psychiatry* 21: 454
- Lupien SJ, McEwen BS, Gunnar MR, Heim C (2009) Effects of stress throughout the lifespan on the brain, behaviour and cognition. *Nature reviews Neuroscience* 10: 434-445

- Lynall ME, McIntosh AM (2023) The Heterogeneity of Depression. *The American journal of psychiatry* 180: 703-704
- MacQueen GM, Yucel K, Taylor VH, Macdonald K, Joffe R (2008) Posterior hippocampal volumes are associated with remission rates in patients with major depressive disorder. *Biological psychiatry* 64: 880-883
- Magarbeh L, Elsheikh SSM, Islam F, Marshe VS, Men X, Tavakoli E, Kronenbuerger M, Kloiber S, Frey BN, Milev R *et al* (2025) Polygenic Risk Score Analysis of Antidepressant Treatment Outcomes: A CAN-BIND-1 Study Report: Analyse des résultats du traitement antidépresseur à l'aide des scores de risque polygéniques : Rapport sur l'étude CAN-BIND-1. *Canadian journal of psychiatry Revue canadienne de psychiatrie*: 7067437251329073
- Maglanoc LA, Landrø NI, Jonassen R, Kaufmann T, Córdova-Palomera A, Hilland E, Westlye LT (2019) Data-Driven Clustering Reveals a Link Between Symptoms and Functional Brain Connectivity in Depression. *Biological psychiatry Cognitive neuroscience and neuroimaging* 4: 16-26
- Maj M, Stein DJ, Parker G, Zimmerman M, Fava GA, De Hert M, Demyttenaere K, McIntyre RS, Widiger T, Wittchen HU (2020) The clinical characterization of the adult patient with depression aimed at personalization of management. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 19: 269-293
- Major Depressive Disorder Working Group of the Psychiatric Genomics Consortium (2025) Trans-ancestry genome-wide study of depression identifies 697 associations implicating cell types and pharmacotherapies. *Cell* 188: 640-652.e649
- Malhi GS, Mann JJ (2018) Depression. *Lancet (London, England)* 392: 2299-2312
- Małujło-Balcerska E, Kumor-Kisiełowska A, Szemraj J, Pietras T (2022) Chemokine (C-C motif) ligand 5 (RANTES) concentrations in the peripheral blood of patients with a depressive disorder. *Pharmacological reports : PR* 74: 759-768
- Malykhin NV, Carter R, Seres P, Coupland NJ (2010) Structural changes in the hippocampus in major depressive disorder: contributions of disease and treatment. *Journal of psychiatry & neuroscience : JPN* 35: 337-343
- Manichaikul A, Mychaleckyj JC, Rich SS, Daly K, Sale M, Chen WM (2010) Robust relationship inference in genome-wide association studies. *Bioinformatics (Oxford, England)* 26: 2867-2873

- Marek S, Laumann TO (2024) Replicability and generalizability in population psychiatric neuroimaging. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 50: 52-57
- Marquand AF, Kia SM, Zabihi M, Wolfers T, Buitelaar JK, Beckmann CF (2019) Conceptualizing mental disorders as deviations from normative functioning. *Molecular psychiatry* 24: 1415-1424
- Marquand AF, Wolfers T, Mennes M, Buitelaar J, Beckmann CF (2016) Beyond Lumping and Splitting: A Review of Computational Approaches for Stratifying Psychiatric Disorders. *Biological psychiatry Cognitive neuroscience and neuroimaging* 1: 433-447
- Marstaller L, Burianová H, Reutens DC (2016) Individual differences in structural and functional connectivity predict speed of emotion discrimination. *Cortex; a journal devoted to the study of the nervous system and behavior* 85: 65-74
- Martin AR, Kanai M, Kamatani Y, Okada Y, Neale BM, Daly MJ (2019) Clinical use of current polygenic risk scores may exacerbate health disparities. *Nature genetics* 51: 584-591
- Martínez-Arán A, Vieta E, Reinares M, Colom F, Torrent C, Sánchez-Moreno J, Benabarre A, Goikolea JM, Comes M, Salamero M (2004) Cognitive function across manic or hypomanic, depressed, and euthymic states in bipolar disorder. *The American journal of psychiatry* 161: 262-270
- McAllister-Williams RH, Arango C, Blier P, Demyttenaere K, Falkai P, Gorwood P, Hopwood M, Javed A, Kasper S, Malhi GS *et al* (2020) The identification, assessment and management of difficult-to-treat depression: An international consensus statement. *Journal of affective disorders* 267: 264-282
- McCarthy S, Das S, Kretzschmar W, Delaneau O, Wood AR, Teumer A, Kang HM, Fuchsberger C, Danecek P, Sharp K *et al* (2016) A reference panel of 64,976 haplotypes for genotype imputation. *Nature genetics* 48: 1279-1283
- McIntyre RS, Alsuwaidan M, Baune BT, Berk M, Demyttenaere K, Goldberg JF, Gorwood P, Ho R, Kasper S, Kennedy SH *et al* (2023) Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 22: 394-412

- McIntyre RS, Berk M, Brietzke E, Goldstein BI, López-Jaramillo C, Kessing LV, Malhi GS, Nierenberg AA, Rosenblat JD, Majeed A *et al* (2020) Bipolar disorders. *Lancet (London, England)* 396: 1841-1856
- McManus E, Haroon H, Duncan NW, Elliott R, Muhlert N (2022) The effects of stress across the lifespan on the brain, cognition and mental health: A UK biobank study. *Neurobiology of stress* 18: 100447
- McWhinney SR, Abé C, Alda M, Benedetti F, Bøen E, Del Mar Bonnin C, Borgers T, Brosch K, Canales-Rodríguez EJ, Cannon DM *et al* (2022) Diagnosis of bipolar disorders and body mass index predict clustering based on similarities in cortical thickness-ENIGMA study in 2436 individuals. *Bipolar disorders* 24: 509-520
- McWhinney SR, Hlinka J, Bakstein E, Dietze LMF, Corkum ELV, Abé C, Alda M, Alexander N, Benedetti F, Berk M *et al* (2024) Principal component analysis as an efficient method for capturing multivariate brain signatures of complex disorders-ENIGMA study in people with bipolar disorders and obesity. *Human brain mapping* 45: e26682
- Meerman JJ, Ter Hark SE, Janzing JGE, Coenen MJH (2022) The Potential of Polygenic Risk Scores to Predict Antidepressant Treatment Response in Major Depression: A Systematic Review. *Journal of affective disorders* 304: 1-11
- Merikangas KR, Akiskal HS, Angst J, Greenberg PE, Hirschfeld RM, Petukhova M, Kessler RC (2007) Lifetime and 12-month prevalence of bipolar spectrum disorder in the National Comorbidity Survey replication. *Archives of general psychiatry* 64: 543-552
- Mesbah R, Koenders MA, van der Wee NJA, Giltay EJ, van Hemert AM, de Leeuw M (2023) Association Between the Fronto-Limbic Network and Cognitive and Emotional Functioning in Individuals With Bipolar Disorder: A Systematic Review and Meta-analysis. *JAMA psychiatry* 80: 432-440
- Meyer-Baese L, Jaeger D, Keilholz S (2025) Neurovascular coupling: a review of spontaneous neocortical dynamics linking neuronal activity to hemodynamics and what we have learned from the rodent brain. *Journal of neurophysiology* 133: 644-660
- Mezuk B, Eaton WW, Albrecht S, Golden SH (2008) Depression and type 2 diabetes over the lifespan: a meta-analysis. *Diabetes care* 31: 2383-2390

- Michellini G, Palumbo IM, DeYoung CG, Latzman RD, Kotov R (2021) Linking RDoC and HiTOP: A new interface for advancing psychiatric nosology and neuroscience. *Clinical psychology review* 86: 102025
- Miguel PM, Pereira LO, Silveira PP, Meaney MJ (2019) Early environmental influences on the development of children's brain structure and function. *Developmental medicine and child neurology* 61: 1127-1133
- Milaneschi Y, Lamers F, Berk M, Penninx B (2020) Depression Heterogeneity and Its Biological Underpinnings: Toward Immunometabolic Depression. *Biological psychiatry* 88: 369-380
- Milaneschi Y, Lamers F, Peyrot WJ, Abdellaoui A, Willemsen G, Hottenga JJ, Jansen R, Mbarek H, Dehghan A, Lu C *et al* (2016) Polygenic dissection of major depression clinical heterogeneity. *Molecular psychiatry* 21: 516-522
- Milaneschi Y, Lamers F, Peyrot WJ, Baune BT, Breen G, Dehghan A, Forstner AJ, Grabe HJ, Homuth G, Kan C *et al* (2017) Genetic Association of Major Depression With Atypical Features and Obesity-Related Immunometabolic Dysregulations. *JAMA psychiatry* 74: 1214-1225
- Milenkovic VM, Stanton EH, Nothdurfter C, Rupprecht R, Wetzel CH (2019) The Role of Chemokines in the Pathophysiology of Major Depressive Disorder. *International journal of molecular sciences* 20
- Miller JN, Black DW (2020) Bipolar Disorder and Suicide: a Review. *Current psychiatry reports* 22: 6
- Milligan GW (1980) An examination of the effect of six types of error perturbation on fifteen clustering algorithms. *Psychometrika* 45: 325-342
- Milligan GW, Cooper MC (1988) A study of standardization of variables in cluster analysis. *Journal of classification* 5: 181-204
- Miola A, Meda N, Perini G, Sambataro F (2023) Structural and functional features of treatment-resistant depression: A systematic review and exploratory coordinate-based meta-analysis of neuroimaging studies. *Psychiatry and clinical neurosciences* 77: 252-263
- Miranda L, Paul R, Pütz B, Koutsouleris N, Müller-Myhsok B (2021) Systematic Review of Functional MRI Applications for Psychiatric Disease Subtyping. *Frontiers in psychiatry* 12: 665536

- Mitchell BL, Monistrol-Mula A, Thomas JT, Byrne EM (2025) The Role of Genetic Data in Dissecting Depression Heterogeneity. *Biological psychiatry*
- Moffitt TE, Caspi A, Rutter M (2005) Strategy for investigating interactions between measured genes and measured environments. *Archives of general psychiatry* 62: 473-481
- Monroe SM, Anderson SF, Harkness KL (2019) Life stress and major depression: The mysteries of recurrences. *Psychological review* 126: 791-816
- Monroe SM, Slavich GM, Torres LD, Gotlib IH (2007) Major life events and major chronic difficulties are differentially associated with history of major depressive episodes. *Journal of abnormal psychology* 116: 116-124
- Montagu JD (1963) HABITUATION OF THE PSYCHO-GALVANIC REFLEX DURING SERIAL TESTS. *Journal of psychosomatic research* 7: 199-214
- Monti S, Tamayo P, Mesirov J, Golub T (2003) Consensus clustering: a resampling-based method for class discovery and visualization of gene expression microarray data. *Machine learning* 52: 91-118
- Moradi Y, Albatineh AN, Mahmoodi H, Gheshlagh RG (2021) The relationship between depression and risk of metabolic syndrome: a meta-analysis of observational studies. *Clinical diabetes and endocrinology* 7: 4
- Moran C, Phan TG, Chen J, Blizzard L, Beare R, Venn A, Münch G, Wood AG, Forbes J, Greenaway TM *et al* (2013) Brain atrophy in type 2 diabetes: regional distribution and influence on cognition. *Diabetes care* 36: 4036-4042
- Moreno-López L, Ioannidis K, Askelund AD, Smith AJ, Schueler K, van Harmelen AL (2020) The Resilient Emotional Brain: A Scoping Review of the Medial Prefrontal Cortex and Limbic Structure and Function in Resilient Adults With a History of Childhood Maltreatment. *Biological psychiatry Cognitive neuroscience and neuroimaging* 5: 392-402
- Mori S, Wakana S, Van Zijl PC, Nagae-Poetscher L (2005) *MRI atlas of human white matter*. Elsevier
- Morimoto SS, Wexler BE, Alexopoulos GS (2012) Neuroplasticity-based computerized cognitive remediation for geriatric depression. *International journal of geriatric psychiatry* 27: 1239-1247

- Morimoto SS, Wexler BE, Liu J, Hu W, Seirup J, Alexopoulos GS (2014) Neuroplasticity-based computerized cognitive remediation for treatment-resistant geriatric depression. *Nature communications* 5: 4579
- Morin RT, Nelson C, Bickford D, Insel PS, Mackin RS (2020) Somatic and anxiety symptoms of depression are associated with disability in late life depression. *Aging & mental health* 24: 1225-1228
- Morrison MC, Kleemann R (2015) Role of Macrophage Migration Inhibitory Factor in Obesity, Insulin Resistance, Type 2 Diabetes, and Associated Hepatic Co-Morbidities: A Comprehensive Review of Human and Rodent Studies. *Frontiers in immunology* 6: 308
- Moylan S, Maes M, Wray NR, Berk M (2013) The neuroprogressive nature of major depressive disorder: pathways to disease evolution and resistance, and therapeutic implications. *Molecular psychiatry* 18: 595-606
- Müller VI, Cieslik EC, Serbanescu I, Laird AR, Fox PT, Eickhoff SB (2017) Altered Brain Activity in Unipolar Depression Revisited: Meta-analyses of Neuroimaging Studies. *JAMA psychiatry* 74: 47-55
- Mullins N, Forstner AJ, O'Connell KS, Coombes B, Coleman JRI, Qiao Z, Als TD, Bigdeli TB, Børte S, Bryois J *et al* (2021) Genome-wide association study of more than 40,000 bipolar disorder cases provides new insights into the underlying biology. *Nature genetics* 53: 817-829
- Murray GK, Lin T, Austin J, McGrath JJ, Hickie IB, Wray NR (2021) Could Polygenic Risk Scores Be Useful in Psychiatry?: A Review. *JAMA psychiatry* 78: 210-219
- Nan X, Li W, Wang L (2024) Functional magnetic resonance imaging studies in bipolar disorder in resting state: A coordinates-based meta-analysis. *Psychiatry research Neuroimaging* 344: 111869
- Nanni V, Uher R, Danese A (2012) Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *The American journal of psychiatry* 169: 141-151
- Nemeroff CB (2016) Paradise Lost: The Neurobiological and Clinical Consequences of Child Abuse and Neglect. *Neuron* 89: 892-909
- Nestler EJ (2014) Epigenetic mechanisms of depression. *JAMA psychiatry* 71: 454-456

- Newson JJ, Hunter D, Thiagarajan TC (2020) The Heterogeneity of Mental Health Assessment. *Frontiers in psychiatry* 11: 76
- Nguyen TD, Harder A, Xiong Y, Kowalec K, Hägg S, Cai N, Kuja-Halkola R, Dalman C, Sullivan PF, Lu Y (2022) Genetic heterogeneity and subtypes of major depression. *Molecular psychiatry* 27: 1667-1675
- Nichols TE, Das S, Eickhoff SB, Evans AC, Glatard T, Hanke M, Kriegeskorte N, Milham MP, Poldrack RA, Poline JB *et al* (2017) Best practices in data analysis and sharing in neuroimaging using MRI. *Nature neuroscience* 20: 299-303
- Nierenberg AA, Agustini B, Köhler-Forsberg O, Cusin C, Katz D, Sylvia LG, Peters A, Berk M (2023) Diagnosis and Treatment of Bipolar Disorder: A Review. *Jama* 330: 1370-1380
- Nievergelt CM, Maihofer AX, Atkinson EG, Chen CY, Choi KW, Coleman JRI, Daskalakis NP, Duncan LE, Polimanti R, Aaronson C *et al* (2024) Genome-wide association analyses identify 95 risk loci and provide insights into the neurobiology of post-traumatic stress disorder. *Nature genetics* 56: 792-808
- Nikpay M, Goel A, Won HH, Hall LM, Willenborg C, Kanoni S, Saleheen D, Kyriakou T, Nelson CP, Hopewell JC *et al* (2015) A comprehensive 1,000 Genomes-based genome-wide association meta-analysis of coronary artery disease. *Nature genetics* 47: 1121-1130
- Nouwen A, Adriaanse MC, van Dam K, Iversen MM, Viechtbauer W, Peyrot M, Caramlau I, Kokoszka A, Kanc K, de Groot M *et al* (2019) Longitudinal associations between depression and diabetes complications: a systematic review and meta-analysis. *Diabetic medicine : a journal of the British Diabetic Association* 36: 1562-1572
- O'Connell KS, Koromina M, van der Veen T, Boltz T, David FS, Yang JMK, Lin KH, Wang X, Coleman JRI, Mitchell BL *et al* (2025) Genomics yields biological and phenotypic insights into bipolar disorder. *Nature* 639: 968-975
- Ogle DH, Doll JC, Powell Wheeler A, Dinno A (2025) *FSA: Simple Fisheries Stock Assessment Methods*
- Ogutu JO, Schulz-Streeck T, Piepho HP (2012) Genomic selection using regularized linear regression models: ridge regression, lasso, elastic net and their extensions. *BMC proceedings* 6 Suppl 2: S10

- Ojala M, Garriga GC (2010) Permutation tests for studying classifier performance. *Journal of machine learning research* 11
- Onyeka I, Collier H, Nåheim EE, Nwaru B, Melle I (2019) Comorbidity of Physical Disorders Among Patients With Severe Mental Illness With and Without Substance Use Disorders: A Systematic Review and Meta-Analysis. *Journal of dual diagnosis* 15: 192-206
- Oraki Kohshour M, Strom NI, Meier SM, McMahon FJ, Merikangas KR, Schulze TG, Mattheisen M (2024) Genetics of Psychiatric Disorders: Advances in Genetic Epidemiology and Genomic Approaches. *Tasman's Psychiatry*: 1-26
- Osimo EF, Baxter LJ, Lewis G, Jones PB, Khandaker GM (2019) Prevalence of low-grade inflammation in depression: a systematic review and meta-analysis of CRP levels. *Psychological medicine* 49: 1958-1970
- Osimo EF, Pillinger T, Rodriguez IM, Khandaker GM, Pariante CM, Howes OD (2020) Inflammatory markers in depression: A meta-analysis of mean differences and variability in 5,166 patients and 5,083 controls. *Brain, behavior, and immunity* 87: 901-909
- Ostojic D, Lalousis PA, Donohoe G, Morris DW (2024) The challenges of using machine learning models in psychiatric research and clinical practice. *European neuropsychopharmacology : the journal of the European College of Neuropsychopharmacology* 88: 53-65
- Palmer DS, Howrigan DP, Chapman SB, Adolfsson R, Bass N, Blackwood D, Boks MPM, Chen CY, Churchhouse C, Corvin AP *et al* (2022) Exome sequencing in bipolar disorder identifies AKAP11 as a risk gene shared with schizophrenia. *Nature genetics* 54: 541-547
- Pan X, Kaminga AC, Wen SW, Liu A (2021) Chemokines in Prediabetes and Type 2 Diabetes: A Meta-Analysis. *Frontiers in immunology* 12: 622438
- Paolucci EM, Loukov D, Bowdish DME, Heisz JJ (2018) Exercise reduces depression and inflammation but intensity matters. *Biological psychology* 133: 79-84
- Park C, Rosenblat JD, Brietzke E, Pan Z, Lee Y, Cao B, Zuckerman H, Kalantarova A, McIntyre RS (2019) Stress, epigenetics and depression: A systematic review. *Neuroscience and biobehavioral reviews* 102: 139-152

- Park YM, Shekhtman T, Kelsoe JR (2020) Effect of the Type and Number of Adverse Childhood Experiences and the Timing of Adverse Experiences on Clinical Outcomes in Individuals with Bipolar Disorder. *Brain sciences* 10
- Pasi M, van Uden IW, Tuladhar AM, de Leeuw FE, Pantoni L (2016) White Matter Microstructural Damage on Diffusion Tensor Imaging in Cerebral Small Vessel Disease: Clinical Consequences. *Stroke* 47: 1679-1684
- Pasquali R, Vicennati V (2000) The abdominal obesity phenotype and insulin resistance are associated with abnormalities of the hypothalamic-pituitary-adrenal axis in humans. *Hormone and metabolic research = Hormon- und Stoffwechselforschung = Hormones et métabolisme* 32: 521-525
- Patenaude B, Smith SM, Kennedy DN, Jenkinson M (2011) A Bayesian model of shape and appearance for subcortical brain segmentation. *NeuroImage* 56: 907-922
- Pavlou M, Ambler G, Seaman S, De Iorio M, Omar RZ (2016) Review and evaluation of penalised regression methods for risk prediction in low-dimensional data with few events. *Statistics in medicine* 35: 1159-1177
- Penke L, Muñoz Maniega S, Murray C, Gow AJ, Hernández MC, Clayden JD, Starr JM, Wardlaw JM, Bastin ME, Deary IJ (2010) A general factor of brain white matter integrity predicts information processing speed in healthy older people. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 30: 7569-7574
- Penner-Goeke S, Binder EB (2019) Epigenetics and depression^[15]. *Dialogues in clinical neuroscience* 21: 397-405
- Penninx B, Lamers F, Jansen R, Berk M, Khandaker GM, De Picker L, Milaneschi Y (2025) Immuno-metabolic depression: from concept to implementation. *The Lancet regional health Europe* 48: 101166
- Pérez-Sola V, Roca M, Alonso J, Gabilondo A, Hernando T, Sicras-Mainar A, Sicras-Navarro A, Herrera B, Vieta E (2021) Economic impact of treatment-resistant depression: A retrospective observational study. *Journal of affective disorders* 295: 578-586
- Perlis RH, Dennehy EB, Miklowitz DJ, Delbello MP, Ostacher M, Calabrese JR, Ametrano RM, Wisniewski SR, Bowden CL, Thase ME *et al* (2009) Retrospective age at onset of bipolar disorder and outcome during two-year follow-up: results from the STEP-BD study. *Bipolar disorders* 11: 391-400

- Petralia MC, Mazzon E, Fagone P, Basile MS, Lenzo V, Quattropani MC, Bendtzen K, Nicoletti F (2020) Pathogenic contribution of the Macrophage migration inhibitory factor family to major depressive disorder and emerging tailored therapeutic approaches. *Journal of affective disorders* 263: 15-24
- Pfeifer JC, Welge J, Strakowski SM, Adler CM, DelBello MP (2008) Meta-analysis of amygdala volumes in children and adolescents with bipolar disorder. *Journal of the American Academy of Child and Adolescent Psychiatry* 47: 1289-1298
- Phillips C, Fahimi A (2018) Immune and Neuroprotective Effects of Physical Activity on the Brain in Depression. *Frontiers in neuroscience* 12: 498
- Pilmeyer J, Huijbers W, Lamerichs R, Jansen JFA, Breeuwer M, Zinger S (2022) Functional MRI in major depressive disorder: A review of findings, limitations, and future prospects. *Journal of neuroimaging : official journal of the American Society of Neuroimaging* 32: 582-595
- Plichta MM, Grimm O, Morgen K, Mier D, Sauer C, Haddad L, Tost H, Esslinger C, Kirsch P, Schwarz AJ *et al* (2014) Amygdala habituation: a reliable fMRI phenotype. *NeuroImage* 103: 383-390
- Poldrack RA, Baker CI, Durnez J, Gorgolewski KJ, Matthews PM, Munafò MR, Nichols TE, Poline JB, Vul E, Yarkoni T (2017) Scanning the horizon: towards transparent and reproducible neuroimaging research. *Nature reviews Neuroscience* 18: 115-126
- Poletti S, Bollettini I, Mazza E, Locatelli C, Radaelli D, Vai B, Smeraldi E, Colombo C, Benedetti F (2015) Cognitive performances associate with measures of white matter integrity in bipolar disorder. *Journal of affective disorders* 174: 342-352
- Poletti S, Mazza MG, Benedetti F (2024) Inflammatory mediators in major depression and bipolar disorder. *Translational psychiatry* 14: 247
- Pompili M, Gonda X, Serafini G, Innamorati M, Sher L, Amore M, Rihmer Z, Girardi P (2013) Epidemiology of suicide in bipolar disorders: a systematic review of the literature. *Bipolar disorders* 15: 457-490
- Pompili M, Innamorati M, Szanto K, Di Vittorio C, Conwell Y, Lester D, Tatarelli R, Girardi P, Amore M (2011) Life events as precipitants of suicide attempts among first-time suicide attempters, repeaters, and non-attempters. *Psychiatry research* 186: 300-305

- Popoli M, Yan Z, McEwen BS, Sanacora G (2011) The stressed synapse: the impact of stress and glucocorticoids on glutamate transmission. *Nature reviews Neuroscience* 13: 22-37
- Post RM (2007) Kindling and sensitization as models for affective episode recurrence, cyclicity, and tolerance phenomena. *Neuroscience and biobehavioral reviews* 31: 858-873
- Post RM, Denicoff KD, Leverich GS, Altshuler LL, Frye MA, Suppes TM, Rush AJ, Keck PE, Jr., McElroy SL, Luckenbaugh DA *et al* (2003) Morbidity in 258 bipolar outpatients followed for 1 year with daily prospective ratings on the NIMH life chart method. *The Journal of clinical psychiatry* 64: 680-690; quiz 738-689
- Price RB, Gates K, Kraynak TE, Thase ME, Siegle GJ (2017a) Data-Driven Subgroups in Depression Derived from Directed Functional Connectivity Paths at Rest. *Neuropsychopharmacology: official publication of the American College of Neuropsychopharmacology* 42: 2623-2632
- Price RB, Lane S, Gates K, Kraynak TE, Horner MS, Thase ME, Siegle GJ (2017b) Parsing Heterogeneity in the Brain Connectivity of Depressed and Healthy Adults During Positive Mood. *Biological psychiatry* 81: 347-357
- Privé F, Arbel J, Vilhjálmsón BJ (2021) LDpred2: better, faster, stronger. *Bioinformatics* 36: 5424-5431.
- Privé F, Arbel J, Aschard H, Vilhjálmsón BJ (2022) Identifying and correcting for misspecifications in GWAS summary statistics and polygenic scores. *Human Genetics and Genomic Advances* 3: 100136.
- Purcell S, Chang C, 2007. PLINK [version 1.9].
- Raichle ME (2015) The brain's default mode network. *Annual review of neuroscience* 38: 433-447
- Rajput D, Wang WJ, Chen CC (2023) Evaluation of a decided sample size in machine learning applications. *BMC bioinformatics* 24: 48
- Reel PS, Reel S, Pearson E, Trucco E, Jefferson E (2021) Using machine learning approaches for multi-omics data analysis: A review. *Biotechnology advances* 49: 107739
- Reginsson GW, Ingason A, Euesden J, Bjornsdottir G, Olafsson S, Sigurdsson E, Oskarsson H, Tyrfinngsson T, Runarsdottir V, Hansdottir I *et al* (2018) Polygenic risk

- scores for schizophrenia and bipolar disorder associate with addiction. *Addiction biology* 23: 485-492
- Repple J, König A, de Lange SC, Opel N, Redlich R, Meinert S, Grotegerd D, Mauritz M, Hahn T, Borgers T *et al* (2022) Association Between Genetic Risk for Type 2 Diabetes and Structural Brain Connectivity in Major Depressive Disorder. *Biological psychiatry Cognitive neuroscience and neuroimaging* 7: 333-340
- Revelle W (2025) psych: Procedures for Psychological, Psychometric, and Personality Research.
- Rhebergen D, Lamers F, Spijker J, de Graaf R, Beekman AT, Penninx BW (2012) Course trajectories of unipolar depressive disorders identified by latent class growth analysis. *Psychological medicine* 42: 1383-1396
- Riera-Serra P, Navarra-Ventura G, Castro A, Gili M, Salazar-Cedillo A, Ricci-Cabello I, Roldán-Espínola L, Coronado-Simsic V, García-Toro M, Gómez-Juanes R *et al* (2024) Clinical predictors of suicidal ideation, suicide attempts and suicide death in depressive disorder: a systematic review and meta-analysis. *European archives of psychiatry and clinical neuroscience* 274: 1543-1563
- Rousseeuw PJ (1987) Silhouettes: a graphical aid to the interpretation and validation of cluster analysis. *Journal of computational applied mathematics* 20: 53-65
- Rowland TA, Marwaha S (2018) Epidemiology and risk factors for bipolar disorder. *Therapeutic advances in psychopharmacology* 8: 251-269
- Rush AJ, Aaronson ST, Demyttenaere K (2019) Difficult-to-treat depression: A clinical and research roadmap for when remission is elusive. *The Australian and New Zealand journal of psychiatry* 53: 109-118
- Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, Niederehe G, Thase ME, Lavori PW, Lebowitz BD *et al* (2006) Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. *The American journal of psychiatry* 163: 1905-1917
- Sackeim HA (2001) The definition and meaning of treatment-resistant depression. *The Journal of clinical psychiatry* 62 Suppl 16: 10-17
- Sah P, Faber ES, Lopez De Armentia M, Power J (2003) The amygdaloid complex: anatomy and physiology. *Physiological reviews* 83: 803-834

- Salimi-Khorshidi G, Douaud G, Beckmann CF, Glasser MF, Griffanti L, Smith SM (2014) Automatic denoising of functional MRI data: combining independent component analysis and hierarchical fusion of classifiers. *NeuroImage* 90: 449-468
- Salk RH, Hyde JS, Abramson LY (2017) Gender differences in depression in representative national samples: Meta-analyses of diagnoses and symptoms. *Psychological bulletin* 143: 783-822
- Saveanu R, Etkin A, Duchemin AM, Goldstein-Piekarski A, Gyurak A, Debatista C, Schatzberg AF, Sood S, Day CV, Palmer DM *et al* (2015) The international Study to Predict Optimized Treatment in Depression (iSPOT-D): outcomes from the acute phase of antidepressant treatment. *Journal of psychiatric research* 61: 1-12
- Scangos KW, State MW, Miller AH, Baker JT, Williams LM (2023) New and emerging approaches to treat psychiatric disorders. *Nature medicine* 29: 317-333
- Schaffer A, Isometsä ET, Tondo L, D HM, Turecki G, Reis C, Cassidy F, Sinyor M, Azorin JM, Kessing LV *et al* (2015) International Society for Bipolar Disorders Task Force on Suicide: meta-analyses and meta-regression of correlates of suicide attempts and suicide deaths in bipolar disorder. *Bipolar disorders* 17: 1-16
- Scheinost D, Noble S, Horien C, Greene AS, Lake EM, Salehi M, Gao S, Shen X, O'Connor D, Barron DS *et al* (2019) Ten simple rules for predictive modeling of individual differences in neuroimaging. *NeuroImage* 193: 35-45
- Schmaal L, Hibar DP, Sämann PG, Hall GB, Baune BT, Jahanshad N, Cheung JW, van Erp TGM, Bos D, Ikram MA *et al* (2017) Cortical abnormalities in adults and adolescents with major depression based on brain scans from 20 cohorts worldwide in the ENIGMA Major Depressive Disorder Working Group. *Molecular psychiatry* 22: 900-909
- Schmaal L, Veltman DJ, van Erp TG, Sämann PG, Frodl T, Jahanshad N, Loehrer E, Tiemeier H, Hofman A, Niessen WJ *et al* (2016) Subcortical brain alterations in major depressive disorder: findings from the ENIGMA Major Depressive Disorder working group. *Molecular psychiatry* 21: 806-812
- Schnellbacher GJ, Rajkumar R, Veselinović T, Ramkiran S, Hagen J, Shah NJ, Neuner I (2022) Structural alterations of the insula in depression patients - A 7-Tesla-MRI study. *NeuroImage Clinical* 36: 103249

- Schuch F, Vancampfort D, Firth J, Rosenbaum S, Ward P, Reichert T, Bagatini NC, Bgeginski R, Stubbs B (2017) Physical activity and sedentary behavior in people with major depressive disorder: A systematic review and meta-analysis. *Journal of affective disorders* 210: 139-150
- Schulz M, Malherbe C, Cheng B, Thomalla G, Schlemm E (2021) Functional connectivity changes in cerebral small vessel disease - a systematic review of the resting-state MRI literature. *BMC medicine* 19: 103
- Schumann G, Benegal V, Yu C, Tao S, Jernigan T, Heinz A, Araya R, Yu L, Calhoun V (2019) Precision medicine and global mental health. *The Lancet Global health* 7: e32
- Schumer MC, Chase HW, Rozovsky R, Eickhoff SB, Phillips ML (2023) Prefrontal, parietal, and limbic condition-dependent differences in bipolar disorder: a large-scale meta-analysis of functional neuroimaging studies. *Molecular psychiatry* 28: 2826-2838
- Seeley WW, Menon V, Schatzberg AF, Keller J, Glover GH, Kenna H, Reiss AL, Greicius MD (2007) Dissociable intrinsic connectivity networks for salience processing and executive control. *The Journal of neuroscience : the official journal of the Society for Neuroscience* 27: 2349-2356
- Serra G, De Crescenzo F, Maisto F, Galante JR, Iannoni ME, Trasolini M, Maglio G, Tondo L, Baldessarini RJ, Vicari S (2022) Suicidal behavior in juvenile bipolar disorder and major depressive disorder patients: Systematic review and meta-analysis. *Journal of affective disorders* 311: 572-581
- Sforzini L, Worrell C, Kose M, Anderson IM, Aouizerate B, Arolt V, Bauer M, Baune BT, Blier P, Cleare AJ *et al* (2022) A Delphi-method-based consensus guideline for definition of treatment-resistant depression for clinical trials. *Molecular psychiatry* 27: 1286-1299
- Shao Y, Cai Y, Tang H, Liu R, Chen B, Chen W, Yuan Y, Zhang Z, Xu Z (2025) Association between polygenic risk scores combined with clinical characteristics and antidepressant efficacy. *Journal of affective disorders* 369: 559-567
- Sheline YI, Gado MH, Price JL (1998) Amygdala core nuclei volumes are decreased in recurrent major depression. *Neuroreport* 9: 2023-2028

- Shen B, Liu B-D, Wang Q, Ji R, 2014. Robust nonnegative matrix factorization via L 1 norm regularization by multiplicative updating rules, 2014 IEEE International Conference on Image Processing (ICIP). IEEE, pp. 5282-5286.
- Shen X, Reus LM, Cox SR, Adams MJ, Liewald DC, Bastin ME, Smith DJ, Deary IJ, Whalley HC, McIntosh AM (2017) Subcortical volume and white matter integrity abnormalities in major depressive disorder: findings from UK Biobank imaging data. *Scientific reports* 7: 5547
- Shu M, Feng S, Liu J (2022) Targeting disrupted rich-club network organization with neuroplasticity-based computerized cognitive remediation in major depressive disorder patients. *Psychiatry research* 316: 114742
- Sigström R, Kowalec K, Jonsson L, Clements CC, Karlsson R, Nordenskjöld A, Pålsson E, Sullivan PF, Landén M (2022) Association Between Polygenic Risk Scores and Outcome of ECT. *The American journal of psychiatry* 179: 844-852
- Sirugo G, Williams SM, Tishkoff SA (2019) The Missing Diversity in Human Genetic Studies. *Cell* 177: 26-31
- Smith DJ, Nicholl BI, Cullen B, Martin D, Ul-Haq Z, Evans J, Gill JM, Roberts B, Gallacher J, Mackay D *et al* (2013) Prevalence and characteristics of probable major depression and bipolar disorder within UK biobank: cross-sectional study of 172,751 participants. *PloS one* 8: e75362
- Smith SM (2002) Fast robust automated brain extraction. *Human brain mapping* 17: 143-155
- Smith SM, Alfaro-Almagro F, Miller KL, 2024. UK Biobank Brain Imaging Documentation.
- Smith SM, Jenkinson M, Johansen-Berg H, Rueckert D, Nichols TE, Mackay CE, Watkins KE, Ciccarelli O, Cader MZ, Matthews PM *et al* (2006) Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. *NeuroImage* 31: 1487-1505
- Smoller JW, Finn CT (2003) Family, twin, and adoption studies of bipolar disorder. *American journal of medical genetics Part C, Seminars in medical genetics* 123c: 48-58

- Song SK, Yoshino J, Le TQ, Lin SJ, Sun SW, Cross AH, Armstrong RC (2005) Demyelination increases radial diffusivity in corpus callosum of mouse brain. *NeuroImage* 26: 132-140
- Souama C, Lamers F, Milaneschi Y, Vinkers CH, Defina S, Garvert L, Stein F, Woofenden T, Brosch K, Dannlowski U *et al* (2023) Depression, cardiometabolic disease, and their co-occurrence after childhood maltreatment: an individual participant data meta-analysis including over 200,000 participants. *BMC medicine* 21: 93
- Stannard S, Berrington A, Fraser SDS, Paranjothy S, Hoyle RB, Owen RK, Akbari A, Shiranirad M, Chiovloni R, Alwan NA (2024) Mapping domains of early life determinants of future multimorbidity across three UK longitudinal cohort studies. *Scientific reports* 14: 21454
- Stegenga BT, Nazareth I, Grobbee DE, Torres-González F, Svab I, Maarros HI, Xavier M, Saldivia S, Bottomley C, King M *et al* (2012) Recent life events pose greatest risk for onset of major depressive disorder during mid-life. *Journal of affective disorders* 136: 505-513
- Stokes PRA, Yalin N, Mantingh T, Colasanti A, Patel R, Bellivier F, Leboyer M, Henry C, Kahn JP, Etain B *et al* (2020) Unipolar mania: Identification and characterisation of cases in France and the United Kingdom. *Journal of affective disorders* 263: 228-235
- Sugaya L, Hasin DS, Olfson M, Lin KH, Grant BF, Blanco C (2012) Child physical abuse and adult mental health: a national study. *Journal of traumatic stress* 25: 384-392
- Suh JS, Schneider MA, Minuzzi L, MacQueen GM, Strother SC, Kennedy SH, Frey BN (2019) Cortical thickness in major depressive disorder: A systematic review and meta-analysis. *Progress in neuro-psychopharmacology & biological psychiatry* 88: 287-302
- Sullivan LE, Fiellin DA, O'Connor PG (2005) The prevalence and impact of alcohol problems in major depression: a systematic review. *The American journal of medicine* 118: 330-341
- Sullivan PF (2010) The psychiatric GWAS consortium: big science comes to psychiatry. *Neuron* 68: 182-186

- Sullivan PF, Kessler RC, Kendler KS (1998) Latent class analysis of lifetime depressive symptoms in the national comorbidity survey. *The American journal of psychiatry* 155: 1398-1406
- Sung SC, Wisniewski SR, Balasubramani GK, Zisook S, Kurian B, Warden D, Trivedi MH, Rush AJ (2013) Does early-onset chronic or recurrent major depression impact outcomes with antidepressant medications? A CO-MED trial report. *Psychological medicine* 43: 945-960
- Supti KF, Asaduzzaman M, Suhee FI, Shahriar M, Islam SMA, Bhuiyan MA, Qusar MS, Islam MR (2023) Elevated Serum Macrophage Migration Inhibitory Factor Levels are Associated With Major Depressive Disorder. *Clinical pathology (Thousand Oaks, Ventura County, Calif)* 16: 2632010x231220841
- Suseelan S, Pinna G (2023) Heterogeneity in major depressive disorder: The need for biomarker-based personalized treatments. *Advances in clinical chemistry* 112: 1-67
- Syan SK, Smith M, Frey BN, Remtulla R, Kapeczinski F, Hall GBC, Minuzzi L (2018) Resting-state functional connectivity in individuals with bipolar disorder during clinical remission: a systematic review. *Journal of psychiatry & neuroscience : JPN* 43: 298-316
- Takeuchi H, Kimura R, Tomita H, Taki Y, Kikuchi Y, Ono C, Yu Z, Matsudaira I, Nouchi R, Yokoyama R *et al* (2021) Polygenic risk score for bipolar disorder associates with divergent thinking and brain structures in the prefrontal cortex. *Human brain mapping* 42: 6028-6037
- Talarowska M (2020) Epigenetic Mechanisms in the Neurodevelopmental Theory of Depression. *Depression research and treatment* 2020: 6357873
- Tang B, Yuan S, Xiong Y, He Q, Larsson SC (2020) Major depressive disorder and cardiometabolic diseases: a bidirectional Mendelian randomisation study. *Diabetologia* 63: 1305-1311
- Tang L, Tang R, Zheng J, Zhao P, Zhu R, Tang Y, Zhang X, Gong X, Wang F (2025) Dissecting biological heterogeneity in major depressive disorder based on neuroimaging subtypes with multi-omics data. *Translational psychiatry* 15: 72
- Tansey KE, Guipponi M, Domenici E, Lewis G, Malafosse A, O'Donovan M, Wendland JR, Lewis CM, McGuffin P, Uher R (2014) Genetic susceptibility for bipolar disorder and response to antidepressants in major depressive disorder. *American*

journal of medical genetics Part B, Neuropsychiatric genetics : the official publication of the International Society of Psychiatric Genetics 165b: 77-83

- Tao H, Fan S, Zhu T, You L, Zheng D, Yan L, Ren M (2023) Psychiatric disorders and Type 2 diabetes mellitus: A bidirectional Mendelian randomization. *European journal of clinical investigation* 53: e13893
- Tao S, Zhang Y, Wang Q, Qiao C, Deng W, Liang S, Wei J, Wei W, Yu H, Li X *et al* (2022) Identifying transdiagnostic biological subtypes across schizophrenia, bipolar disorder, and major depressive disorder based on lipidomics profiles. *Frontiers in cell and developmental biology* 10: 969575
- Taylor WD, Aizenstein HJ, Alexopoulos GS (2013) The vascular depression hypothesis: mechanisms linking vascular disease with depression. *Molecular psychiatry* 18: 963-974
- Teicher MH, Samson JA (2013) Childhood maltreatment and psychopathology: A case for ecophenotypic variants as clinically and neurobiologically distinct subtypes. *The American journal of psychiatry* 170: 1114-1133
- Teicher MH, Samson JA, Anderson CM, Ohashi K (2016) The effects of childhood maltreatment on brain structure, function and connectivity. *Nature reviews Neuroscience* 17: 652-666
- Teixeira AL, Martins LB, Berk M, Bauer ME (2022) Severe psychiatric disorders and general medical comorbidities: inflammation-related mechanisms and therapeutic opportunities. *Clinical science (London, England : 1979)* 136: 1257-1280
- Ten Have M, Penninx B, Tuithof M, van Dorsselaer S, Kleinjan M, Spijker J, de Graaf R (2017) Duration of major and minor depressive episodes and associated risk indicators in a psychiatric epidemiological cohort study of the general population. *Acta psychiatrica Scandinavica* 136: 300-312
- Tesen H, Watanabe K, Okamoto N, Ikenouchi A, Igata R, Konishi Y, Kakeda S, Yoshimura R (2021) Volume of Amygdala Subregions and Clinical Manifestations in Patients With First-Episode, Drug-Naïve Major Depression. *Frontiers in human neuroscience* 15: 780884
- Thalamuthu A, Mills NT, Berger K, Minnerup H, Grotegerd D, Dannlowski U, Meinert S, Opel N, Reppe J, Gruber M *et al* (2022) Genome-wide interaction study with

- major depression identifies novel variants associated with cognitive function. *Molecular psychiatry* 27: 1111-1119
- Thase M, Connolly KRJWU (2019) Unipolar depression in adults: Choosing treatment for resistant depression.
- Thase ME, Rush AJ (1997) When at first you don't succeed: sequential strategies for antidepressant nonresponders. *The Journal of clinical psychiatry* 58 Suppl 13: 23-29
- Toenders YJ, van Velzen LS, Heideman IZ, Harrison BJ, Davey CG, Schmaal L (2019) Neuroimaging predictors of onset and course of depression in childhood and adolescence: A systematic review of longitudinal studies. *Developmental cognitive neuroscience* 39: 100700
- Tokuda T, Yoshimoto J, Shimizu Y, Okada G, Takamura M, Okamoto Y, Yamawaki S, Doya K (2018) Identification of depression subtypes and relevant brain regions using a data-driven approach. *Scientific reports* 8: 14082
- Torchiano M (2020) Package ‘effsize’.
- Tozzi L, Zhang X, Chesnut M, Holt-Gosselin B, Ramirez CA, Williams LM (2021) Reduced functional connectivity of default mode network subsystems in depression: Meta-analytic evidence and relationship with trait rumination. *NeuroImage Clinical* 30: 102570
- Tozzi L, Zhang X, Pines A, Olmsted AM, Zhai ES, Anene ET, Chesnut M, Holt-Gosselin B, Chang S, Stetz PC *et al* (2024) Personalized brain circuit scores identify clinically distinct biotypes in depression and anxiety. *Nature medicine* 30: 2076-2087
- Treuer T, Tohen M (2010) Predicting the course and outcome of bipolar disorder: a review. *European psychiatry : the journal of the Association of European Psychiatrists* 25: 328-333
- Trivedi MH, Rush AJ, Wisniewski SR, Nierenberg AA, Warden D, Ritz L, Norquist G, Howland RH, Lebowitz B, McGrath PJ *et al* (2006) Evaluation of outcomes with citalopram for depression using measurement-based care in STAR*D: implications for clinical practice. *The American journal of psychiatry* 163: 28-40
- Trubetskoy V, Pardiñas AF, Qi T, Panagiotaropoulou G, Awasthi S, Bigdeli TB, Bryois J, Chen CY, Dennison CA, Hall LS *et al* (2022) Mapping genomic loci implicates genes and synaptic biology in schizophrenia. *Nature* 604: 502-508

- Tuladhar AM, van Norden AG, de Laat KF, Zwiers MP, van Dijk EJ, Norris DG, de Leeuw FE (2015) White matter integrity in small vessel disease is related to cognition. *NeuroImage Clinical* 7: 518-524
- Turken A, Whitfield-Gabrieli S, Bammer R, Baldo JV, Dronkers NF, Gabrieli JD (2008) Cognitive processing speed and the structure of white matter pathways: convergent evidence from normal variation and lesion studies. *NeuroImage* 42: 1032-1044
- UK Biobank, 2014. MRI acquisition protocols.
- UK Biobank, 2025. Research Analysis Platform.
- Vai B, Bertocchi C, Benedetti F (2019) Cortico-limbic connectivity as a possible biomarker for bipolar disorder: where are we now? *Expert review of neurotherapeutics* 19: 159-172
- Vai B, Calesella F, Lenti C, Fortaner-Uyà L, Caselani E, Fiore P, Breit S, Poletti S, Colombo C, Zanardi R *et al* (2023) Reduced corticolimbic habituation to negative stimuli characterizes bipolar depressed suicide attempters. *Psychiatry research Neuroimaging* 331: 111627
- van Dellen E (2024) Precision psychiatry: predicting predictability. *Psychological medicine* 54: 1500-1509
- van den Heuvel MP, Sporns O (2019) A cross-disorder connectome landscape of brain dysconnectivity. *Nature reviews Neuroscience* 20: 435-446
- van Velzen LS, Kelly S, Isaev D, Aleman A, Aftanas LI, Bauer J, Baune BT, Brak IV, Carballedo A, Connolly CG *et al* (2020) White matter disturbances in major depressive disorder: a coordinated analysis across 20 international cohorts in the ENIGMA MDD working group. *Molecular psychiatry* 25: 1511-1525
- Vancampfort D, Stubbs B, Mitchell AJ, De Hert M, Wampers M, Ward PB, Rosenbaum S, Correll CU (2015) Risk of metabolic syndrome and its components in people with schizophrenia and related psychotic disorders, bipolar disorder and major depressive disorder: a systematic review and meta-analysis. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 14: 339-347
- VandeBunte AM, Fonseca C, Paolillo EW, Gontrum E, Lee SY, Kramer JH, Casaletto KB (2023) Regional Vulnerability of the Corpus Callosum in the Context of Cardiovascular Risk. *Journal of geriatric psychiatry and neurology* 36: 397-406

- Varoquaux G (2018) Cross-validation failure: Small sample sizes lead to large error bars. *NeuroImage* 180: 68-77
- Verma A, Huffman JE, Rodriguez A, Conery M, Liu M, Ho YL, Kim Y, Heise DA, Guare L, Panickan VA *et al* (2024) Diversity and scale: Genetic architecture of 2068 traits in the VA Million Veteran Program. *Science (New York, NY)* 385: eadj1182
- Victor TA, Khalsa SS, Simmons WK, Feinstein JS, Savitz J, Aupperle RL, Yeh HW, Bodurka J, Paulus MP (2018) Tulsa 1000: a naturalistic study protocol for multilevel assessment and outcome prediction in a large psychiatric sample. *BMJ open* 8: e016620
- Vieira R, Faria AR, Ribeiro D, Picó-Pérez M, Bessa JM (2023) Structural and functional brain correlates of suicidal ideation and behaviors in depression: A scoping review of MRI studies. *Progress in neuro-psychopharmacology & biological psychiatry* 126: 110799
- Vieira S, Pinaya WH, Mechelli A (2017) Using deep learning to investigate the neuroimaging correlates of psychiatric and neurological disorders: Methods and applications. *Neuroscience and biobehavioral reviews* 74: 58-75
- Wakana S, Caprihan A, Panzenboeck MM, Fallon JH, Perry M, Gollub RL, Hua K, Zhang J, Jiang H, Dubey P *et al* (2007) Reproducibility of quantitative tractography methods applied to cerebral white matter. *NeuroImage* 36: 630-644
- Wallstrom G, Anderson KS, LaBaer J (2013) Biomarker discovery for heterogeneous diseases. *Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology* 22: 747-755
- Walter K, Min JL, Huang J, Crooks L, Memari Y, McCarthy S, Perry JR, Xu C, Futema M, Lawson D *et al* (2015) The UK10K project identifies rare variants in health and disease. *Nature* 526: 82-90
- Walters RK, Polimanti R, Johnson EC, McClintick JN, Adams MJ, Adkins AE, Aliev F, Bacanu SA, Batzler A, Bertelsen S *et al* (2018) Transancestral GWAS of alcohol dependence reveals common genetic underpinnings with psychiatric disorders. *Nature neuroscience* 21: 1656-1669

- Wang X, Su Y, Liu Q, Li M, Zeighami Y, Fan J, Adams GC, Tan C, Zhu X, Meng X (2025) Unveiling diverse clinical symptom patterns and neural activity profiles in major depressive disorder subtypes. *EBioMedicine* 116: 105756
- Wang Z, He D, Yang L, Wang P, Zou Z, Xiao J, Min W, He Y, Zhu H (2023) Common and distinct patterns of task-related neural activation abnormalities in patients with remitted and current major depressive disorder: A systematic review and coordinate-based meta-analysis. *Neuroscience and biobehavioral reviews* 152: 105284
- Wang Z, Li T, Li S, Li K, Jiang X, Wei C, Yang L, Cao H, Li S, Li J (2022) The prevalence and clinical correlates of medical disorders comorbidities in patients with bipolar disorder. *BMC psychiatry* 22: 176
- Ward J, Graham N, Strawbridge RJ, Ferguson A, Jenkins G, Chen W, Hodgson K, Frye M, Weinshilboum R, Uher R *et al* (2018) Polygenic risk scores for major depressive disorder and neuroticism as predictors of antidepressant response: Meta-analysis of three treatment cohorts. *PloS one* 13: e0203896
- Warren HR, Evangelou E, Cabrera CP, Gao H, Ren M, Mifsud B, Ntalla I, Surendran P, Liu C, Cook JP *et al* (2017) Genome-wide association analysis identifies novel blood pressure loci and offers biological insights into cardiovascular risk. *Nature genetics* 49: 403-415
- Watson HJ, Yilmaz Z, Thornton LM, Hübel C, Coleman JRI, Gaspar HA, Bryois J, Hinney A, Leppä VM, Mattheisen M *et al* (2019) Genome-wide association study identifies eight risk loci and implicates metabo-psychiatric origins for anorexia nervosa. *Nature genetics* 51: 1207-1214
- Weir RA, Rapaport MH (2022) The Relationship Between Major Depressive Disorder and Multiple Medical Conditions: A Call to Improve Integrated Care Services. *The Journal of clinical psychiatry* 83
- Wickham HJRpv (2015) dplyr: A grammar of data manipulation. 3: p156
- Willems SM, Ng NHJ, Fernandez J, Fine RS, Wheeler E, Wessel J, Kitajima H, Marenne G, Sim X, Yaghootkar H *et al* (2023) Large-scale exome array summary statistics resources for glycemic traits to aid effector gene prioritization. *Wellcome open research* 8: 483

- Williams LM, Carpenter WT, Carretta C, Papanastasiou E, Vaidyanathan U (2024) Precision psychiatry and Research Domain Criteria: Implications for clinical trials and future practice. *CNS spectrums* 29: 26-39
- Williams LM, Hack LM (2021) Part 1: Neuroimaging of Circuits. In: *Precision psychiatry: Using neuroscience insights to inform personally tailored, measurement-based care*, American Psychiatric Pub:
- Williams LM, Korgaonkar MS, Song YC, Paton R, Eagles S, Goldstein-Piekarski A, Grieve SM, Harris AW, Usherwood T, Etkin A (2015) Amygdala Reactivity to Emotional Faces in the Prediction of General and Medication-Specific Responses to Antidepressant Treatment in the Randomized iSPOT-D Trial. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* 40: 2398-2408
- Winklewski PJ, Sabisz A, Naumczyk P, Jodzio K, Szurowska E, Szarmach A (2018) Understanding the Physiopathology Behind Axial and Radial Diffusivity Changes-What Do We Know? *Frontiers in neurology* 9: 92
- Wise T, Radua J, Nortje G, Cleare AJ, Young AH, Arnone D (2016) Voxel-Based Meta-Analytical Evidence of Structural Disconnectivity in Major Depression and Bipolar Disorder. *Biological psychiatry* 79: 293-302
- Wium-Andersen MK, Wium-Andersen IK, Prescott EIB, Overvad K, Jørgensen MB, Osler M (2020) An attempt to explain the bidirectional association between ischaemic heart disease, stroke and depression: a cohort and meta-analytic approach. *The British journal of psychiatry : the journal of mental science* 217: 434-441
- Woo CW, Chang LJ, Lindquist MA, Wager TD (2017) Building better biomarkers: brain models in translational neuroimaging. *Nature neuroscience* 20: 365-377
- Woo YS, Rosenblat JD, Kakar R, Bahk WM, McIntyre RS (2016) Cognitive Deficits as a Mediator of Poor Occupational Function in Remitted Major Depressive Disorder Patients. *Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology* 14: 1-16
- Woolrich MW, Ripley BD, Brady M, Smith SM (2001) Temporal autocorrelation in univariate linear modeling of FMRI data. *NeuroImage* 14: 1370-1386
- World Health Organization, 2019. International Classification of Diseases, Eleventh Revision (ICD-11).

- Wray NR, Ripke S, Mattheisen M, Trzaskowski M, Byrne EM, Abdellaoui A, Adams MJ, Agerbo E, Air TM, Andlauer TMF *et al* (2018) Genome-wide association analyses identify 44 risk variants and refine the genetic architecture of major depression. *Nature genetics* 50: 668-681
- Wrobel AL, Köhler-Forsberg O, Sylvia LG, Russell SE, Dean OM, Cotton SM, Thase M, Calabrese JR, Deckersbach T, Tohen M *et al* (2022) Childhood trauma and treatment outcomes during mood-stabilising treatment with lithium or quetiapine among outpatients with bipolar disorder. *Acta psychiatrica Scandinavica* 145: 615-627
- Xu Y, Cheng X, Li Y, Shen H, Wan Y, Ping L, Yu H, Cheng Y, Xu X, Cui J *et al* (2024) Shared and Distinct White Matter Alterations in Major Depression and Bipolar Disorder: A Systematic Review and Meta-Analysis. *Journal of integrative neuroscience* 23: 170
- Yang S, Zhou Y, Wang F, He X, Cui X, Cai S, Zhu X, Wang D (2024) Diffusion tensor imaging in cerebral small vessel disease applications: opportunities and challenges. *Frontiers in neuroscience* 18: 1473462
- Yatham LN, Kennedy SH, Parikh SV, Schaffer A, Bond DJ, Frey BN, Sharma V, Goldstein BI, Rej S, Beaulieu S (2018) Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) 2018 guidelines for the management of patients with bipolar disorder. *Bipolar disorders* 20: 97-170
- Yeo BT, Krienen FM, Sepulcre J, Sabuncu MR, Lashkari D, Hollinshead M, Roffman JL, Smoller JW, Zöllei L, Polimeni JR *et al* (2011) The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *Journal of neurophysiology* 106: 1125-1165
- Yu C, Arcos-Burgos M, Baune BT, Arolt V, Dannlowski U, Wong ML, Licinio J (2018) Low-frequency and rare variants may contribute to elucidate the genetics of major depressive disorder. *Translational psychiatry* 8: 70
- Zajkowska Z, Gullett N, Walsh A, Zonca V, Pedersen GA, Souza L, Kieling C, Fisher HL, Kohrt BA, Mondelli V (2022) Cortisol and development of depression in adolescence and young adulthood - a systematic review and meta-analysis. *Psychoneuroendocrinology* 136: 105625

- Zetin M, Hoepner CT (2007) Relevance of exclusion criteria in antidepressant clinical trials: a replication study. *Journal of clinical psychopharmacology* 27: 295-301
- Zhang H, Li L, Wu M, Chen Z, Hu X, Chen Y, Zhu H, Jia Z, Gong Q (2016) Brain gray matter alterations in first episodes of depression: A meta-analysis of whole-brain studies. *Neuroscience and biobehavioral reviews* 60: 43-50
- Zhang M, Chen J, Yin Z, Wang L, Peng L (2021) The association between depression and metabolic syndrome and its components: a bidirectional two-sample Mendelian randomization study. *Translational psychiatry* 11: 633
- Zhang T, Shaw M, Cherbuin N (2022a) Association between Type 2 Diabetes Mellitus and Brain Atrophy: A Meta-Analysis. *Diabetes & metabolism journal* 46: 781-802
- Zhang X, Liang C, Feng M, Xin H, Fu Y, Gao Y, Sui C, Wang N, Wang Y, Zhang N *et al* (2024) Aberrant brain structural-functional connectivity coupling associated with cognitive dysfunction in different cerebral small vessel disease burdens. *CNS neuroscience & therapeutics* 30: e70005
- Zhang Y, Brady M, Smith S (2001) Segmentation of brain MR images through a hidden Markov random field model and the expectation-maximization algorithm. *IEEE transactions on medical imaging* 20: 45-57
- Zhang Y, Zhang Y, Ai H, Van Dam NT, Qian L, Hou G, Xu P (2022b) Microstructural deficits of the thalamus in major depressive disorder. *Brain communications* 4: fcac236
- Zhao H, Ma Q, Xie M, Huang Y, Liu Y, Song H, Gui H, Li M, Wang Q (2023) Self-rated health as a predictor of hospitalizations in patients with bipolar disorder or major depressive disorder: A prospective cohort study of the UK Biobank. *Journal of affective disorders* 331: 200-206
- Zhao H, Wang F, Luo GH, Lei H, Peng F, Ren QP, Chen W, Wu YF, Yin LC, Liu JC *et al* (2022) Assessment of structural brain changes in patients with type 2 diabetes mellitus using the MRI-based brain atrophy and lesion index. *Neural regeneration research* 17: 618-624
- Zhao JL, Jiang WT, Wang X, Cai ZD, Liu ZH, Liu GR (2020) Exercise, brain plasticity, and depression. *CNS neuroscience & therapeutics* 26: 885-895
- Zheng KZ, Wang HN, Liu J, Xi YB, Li L, Zhang X, Li JM, Yin H, Tan QR, Lu HB *et al* (2018) Incapacity to control emotion in major depression may arise from disrupted

- white matter integrity and OFC-amygdala inhibition. *CNS neuroscience & therapeutics* 24: 1053-1062
- Zhou C, Li J, Dong M, Ping L, Lin H, Wang Y, Wang S, Gao S, Yu G, Cheng Y *et al* (2021) Altered White Matter Microstructures in Type 2 Diabetes Mellitus: A Coordinate-Based Meta-Analysis of Diffusion Tensor Imaging Studies. *Frontiers in endocrinology* 12: 658198
- Zhu Z, Zhao Y, Wen K, Li Q, Pan N, Fu S, Li F, Radua J, Vieta E, Kemp GJ *et al* (2022) Cortical thickness abnormalities in patients with bipolar disorder: A systematic review and meta-analysis. *Journal of affective disorders* 300: 209-218
- Zimmerman M, Chelminski I, Posternak MA (2004) Exclusion criteria used in antidepressant efficacy trials: consistency across studies and representativeness of samples included. *The Journal of nervous and mental disease* 192: 87-94
- Zimmerman M, Ellison W, Young D, Chelminski I, Dalrymple K (2015) How many different ways do patients meet the diagnostic criteria for major depressive disorder? *Comprehensive psychiatry* 56: 29-34
- Zimmerman M, Mattia JJ, Posternak MA (2002) Are subjects in pharmacological treatment trials of depression representative of patients in routine clinical practice? *The American journal of psychiatry* 159: 469-473
- Zisook S, Rush AJ, Lesser I, Wisniewski SR, Trivedi M, Husain MM, Balasubramani GK, Alpert JE, Fava M (2007) Preadult onset vs. adult onset of major depressive disorder: a replication study. *Acta psychiatrica Scandinavica* 115: 196-205
- Zou H, Hastie T (2005) Regularization and variable selection via the elastic net. *Journal of the Royal Statistical Society Series B: Statistical Methodology* 67: 301-320



Appendix

Table A1. Full list of variables included in each stratification model.

Feature category	Variable name	Field ID or definition	Variable type and coding	Dataset
GM	Area of caudalanteriorcingulate (L and R)	27143, 27236	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of caudalmiddlefrontal (L and R)	27144, 27237	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of cuneus (L and R)	27145, 27238	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of entorhinal (L and R)	27146, 27239	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of fusiform (L and R)	27147, 27240	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of inferiorparietal (L and R)	27148, 27241	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of inferiortemporal (L and R)	27149, 27242	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of insula (L and R)	27173, 27266	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of isthmuscingulate (L and R)	27150, 27243	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of lateraloccipital (L and R)	27151, 27244	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of lateralorbitofrontal (L and R)	27152, 27245	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of lingual (L and R)	27153, 27246	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of medialorbitofrontal (L and R)	27154, 27247	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of middletemporal (L and R)	27155, 27248	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of paracentral (L and R)	27157, 27250	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of parahippocampal (L and R)	27156, 27249	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of parsopercularis (L and R)	27158, 27251	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of parsorbitalis (L and R)	27159, 27252	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of parstriangularis (L and R)	27160, 27253	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of pericalcarine (L and R)	27161, 27254	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of postcentral (L and R)	27162, 27255	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of posteriorcingulate (L and R)	27163, 27256	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of precentral (L and R)	27164, 27257	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of precuneus (L and R)	27165, 27258	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of rostralanteriorcingulate (L and R)	27166, 27259	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of rostralmiddlefrontal (L and R)	27167, 27260	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of superiorfrontal (L and R)	27168, 27261	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of superiorparietal (L and R)	27169, 27262	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of superiortemporal (L and R)	27170, 27263	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of supramarginal (L and R)	27171, 27264	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Area of transversetemporal (L and R)	27172, 27265	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

Volume of caudalanteriorcingulate (L and R)	27205, 27298	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of caudalmiddlefrontal (L and R)	27206, 27299	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of cuneus (L and R)	27207, 27300	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of entorhinal (L and R)	27208, 27301	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of fusiform (L and R)	27209, 27302	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of inferiorparietal (L and R)	27210, 27303	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of inferiortemporal (L and R)	27211, 27304	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of insula (L and R)	27235, 27328	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of isthmuscingulate (L and R)	27212, 27305	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of lateraloccipital (L and R)	27213, 27306	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of lateralorbitofrontal (L and R)	27214, 27307	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of lingual (L and R)	27215, 27308	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of medialorbitofrontal (L and R)	27216, 27309	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of middletemporal (L and R)	27217, 27310	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of paracentral (L and R)	27219, 27312	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of parahippocampal (L and R)	27218, 27311	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of parsopercularis (L and R)	27220, 27313	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of parsorbitalis (L and R)	27221, 27314	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of parstriangularis (L and R)	27222, 27315	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of pericalcarine (L and R)	27223, 27316	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of postcentral (L and R)	27224, 27317	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of posteriorcingulate (L and R)	27225, 27318	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of precentral (L and R)	27226, 27319	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of precuneus (L and R)	27227, 27320	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of rostralanteriorcingulate (L and R)	27228, 27321	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of rostralmiddlefrontal (L and R)	27229, 27322	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of superiorfrontal (L and R)	27230, 27323	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of superiorparietal (L and R)	27231, 27324	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of superiortemporal (L and R)	27232, 27325	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of supramarginal (L and R)	27233, 27326	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of transversetemporal (L and R)	27234, 27327	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of caudalanteriorcingulate (L and R)	27174, 27267	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of caudalmiddlefrontal (L and R)	27175, 27268	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of cuneus (L and R)	27176, 27269	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of entorhinal (L and R)	27177, 27270	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

Mean thickness of fusiform (L and R)	27178, 27271	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of inferiorparietal (L and R)	27179, 27272	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of inferiortemporal (L and R)	27180, 27273	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of insula (L and R)	27204, 27297	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of isthmuscingulate (L and R)	27181, 27274	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of lateraloccipital (L and R)	27182, 27275	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of lateralorbitofrontal (L and R)	27183, 27276	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of lingual (L and R)	27184, 27277	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of medialorbitofrontal (L and R)	27185, 27278	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of middletemporal (L and R)	27186, 27279	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of paracentral (L and R)	27188, 27281	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of parahippocampal (L and R)	27187, 27280	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of parsopercularis (L and R)	27189, 27282	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of parsorbitalis (L and R)	27190, 27283	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of parstriangularis (L and R)	27191, 27284	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of pericalcarine (L and R)	27192, 27285	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of postcentral (L and R)	27193, 27286	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of posteriorcingulate (L and R)	27194, 27287	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of precentral (L and R)	27195, 27288	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of precuneus (L and R)	27196, 27289	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of rostralanteriorcingulate (L and R)	27197, 27290	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of rostralmiddlefrontal (L and R)	27198, 27291	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of superiorfrontal (L and R)	27199, 27292	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of superiorparietal (L and R)	27200, 27293	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of superiortemporal (L and R)	27201, 27294	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of supramarginal (L and R)	27202, 27295	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean thickness of transversetemporal (L and R)	27203, 27296	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of accumbens (L and R)	25023, 25024	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of amygdala (L and R)	25021, 25022	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of caudate (L and R)	25013, 25014	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of hippocampus (L and R)	25019, 25020	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of pallidum (L and R)	25017, 25018	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of putamen (L and R)	25015, 25016	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Volume of thalamus (L and R)	25011, 25012	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

DTI	Mean FA in anterior corona radiata (L and R)	25079, 25078	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in anterior limb of internal capsule (L and R)	25073, 25072	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in body of corpus callosum	25059	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in cerebral peduncle (L and R)	25071, 25070	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in cingulum cingulate gyrus (L and R)	25091, 25090	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in cingulum hippocampus (L and R)	25093, 25092	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in corticospinal tract (L and R)	25063, 25062	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in external capsule (L and R)	25089, 25088	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in fornix cres+stria terminalis (L and R)	25095, 25094	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in fornix	25061	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in genu of corpus callosum	25058	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in inferior cerebellar peduncle (L and R)	25067, 25066	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in medial lemniscus (L and R)	25065, 25064	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in middle cerebellar peduncle	25056	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in pontine crossing tract	25057	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in posterior corona radiata (L and R)	25083, 25082	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in posterior limb of internal capsule (L and R)	25075, 25074	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in posterior thalamic radiation (L and R)	25085, 25084	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in retrolenticular part of internal capsule (L and R)	25077, 25076	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in sagittal stratum (L and R)	25087, 25086	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in splenium of corpus callosum	25060	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in superior cerebellar peduncle (L and R)	25069, 25068	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in superior corona radiata (L and R)	25081, 25080	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in superior fronto-occipital fasciculus (L and R)	25099, 25098	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in superior longitudinal fasciculus (L and R)	25097, 25096	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in tapetum (L and R)	25103, 25102	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean FA in uncinate fasciculus (L and R)	25101, 25100	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in anterior corona radiata (L and R)	25223, 25222	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in anterior limb of internal capsule (L and R)	25217, 25216	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in body of corpus callosum	25203	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in cerebral peduncle (L and R)	25215, 25214	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in cingulum cingulate gyrus (L and R)	25235, 25234	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in cingulum hippocampus (L and R)	25237, 25236	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in corticospinal tract (L and R)	25207, 25206	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean AD in external capsule (L and R)	25233, 25232	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

Mean AD in fornix cres+stria terminalis (L and R)	25239, 25238	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in fornix	25205	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in genu of corpus callosum	25202	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in inferior cerebellar peduncle (L and R)	25211, 25210	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in medial lemniscus (L and R)	25209, 25208	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in middle cerebellar peduncle	25200	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in pontine crossing tract	25201	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in posterior corona radiata (L and R)	25227, 25226	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in posterior limb of internal capsule (L and R)	25219, 25218	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in posterior thalamic radiation (L and R)	25229, 25228	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in retrolenticular part of internal capsule (L and R)	25221, 25220	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in sagittal stratum (L and R)	25231, 25230	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in splenium of corpus callosum	25204	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in superior cerebellar peduncle (L and R)	25213, 25212	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in superior corona radiata (L and R)	25225, 25224	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in superior fronto-occipital fasciculus (L and R)	25243, 25242	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in superior longitudinal fasciculus (L and R)	25241, 25240	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in tapetum (L and R)	25247, 25246	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean AD in uncinate fasciculus (L and R)	25245, 25244	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in anterior corona radiata (L and R)	Mean of 25271-25319, and 25270-25318	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in anterior limb of internal capsule (L and R)	Mean of 25265-25313, and 25264-25312	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in body of corpus callosum	Mean of 25251-25299	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in cerebral peduncle (L and R)	Mean of 25263-25311, and 25262-25310	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in cingulum cingulate gyrus (L and R)	Mean of 25283-25331, and 25282-25330	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in cingulum hippocampus (L and R)	Mean of 25285-25333, and 25284-25332	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in corticospinal tract (L and R)	Mean of 25255-25303, and 25254-25302	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in external capsule (L and R)	Mean of 25281-25329, and 25280-25328	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in fornix cres+stria terminalis (L and R)	Mean of 25287-25335, and 25286-25334	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in fornix	Mean of 25253-25301	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in genu of corpus callosum	Mean of 25250-25298	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in inferior cerebellar peduncle (L and R)	Mean of 25259-25307, and 25258-25306	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in medial lemniscus (L and R)	Mean of 25257-25305, and 25256-25304	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in middle cerebellar peduncle	Mean of 25248-25296	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in pontine crossing tract	Mean of 25249-25297	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Mean RD in posterior corona radiata (L and R)	Mean of 25275-25323, and 25274-25322	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

	Mean RD in posterior limb of internal capsule (L and R)	Mean of 25267-25315, and 25266-25314	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in posterior thalamic radiation (L and R)	Mean of 25277-25325, and 25276-25324	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in retrolenticular part of internal capsule (L and R)	Mean of 25269-25317, and 25268-25316	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in sagittal stratum (L and R)	Mean of 25279-25327, and 25278-25326	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in splenium of corpus callosum	Mean of 25252-25300	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in superior cerebellar peduncle (L and R)	Mean of 25261-25309, and 25260-25308	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in superior corona radiata (L and R)	Mean of 25273-25321, and 25272-25320	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in superior fronto-occipital fasciculus (L and R)	Mean of 25291-25339, and 25290-25338	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in superior longitudinal fasciculus (L and R)	Mean of 25289-25337, and 25288-25336	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in tapetum (L and R)	Mean of 25295-25343, and 25294-25342	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in uncinate fasciculus (L and R)	Mean of 25293-25341, and 25292-25340	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Mean RD in tapetum (L and R)	Mean of 25295-25343, and 25294-25342	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
t-fMRI	Median z-statistic (in group-defined amygdala activation mask) for faces-shapes contrast	25054	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Median z-statistic (in group-defined mask) for faces activation	25046	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Median z-statistic (in group-defined mask) for shapes activation	25042	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Median z-statistic (in group-defined mask) for faces-shapes contrast	25050	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	90th percentile of z-statistic (in group-defined amygdala activation mask) for faces-shapes contrast	25768	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	90th percentile of z-statistic (in group-defined mask) for faces activation	25764	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	90th percentile of z-statistic (in group-defined mask) for shapes activation	25762	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	90th percentile of z-statistic (in group-defined mask) for faces-shapes contrast	25766	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Amygdala L habituation for faces condition	Derived from 20249	Continuous	UKB (dMDD), OSR (MDD and BD)
	Amygdala R habituation for faces condition	Derived from 20249	Continuous	UKB (dMDD), OSR (MDD and BD)
	Amygdala L habituation for shapes condition	Derived from 20249	Continuous	UKB (dMDD), OSR (MDD and BD)
	Amygdala R habituation for shapes condition	Derived from 20249	Continuous	UKB (dMDD), OSR (MDD and BD)
rs-fMRI	Strength of positive resting-state connections for each of the 55 ICA components	Derived from 25753	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	Strength of negative resting-state connections for each of the 55 ICA components	Derived from 25753	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
PGSs	PGS for MDD	Derived from MDD PGC (2025)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for BD	Derived from O'Connell et al. (2025)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for SCZ	Derived from Trubetskov et al. (2022)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for ADHD	Derived from Demontis et al. (2023)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for anorexia nervosa	Derived from Watson et al. (2019)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)

	PGS for autism	Derived from Grove et al. (2019)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for alcohol dependence	Derived from Walters et al. (2018)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for CUD	Derived from Johnson et al. (2020)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for generalized anxiety disorder	Derived from Kurki et al. (2023)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for neuroticism	Derived from de Moor et al. (2015)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for OCD	Derived from IOCDF-GC and OCGAS (2018)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for PTSD	Derived from Nievergelt et al. (2024)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for education	Derived from Lee et al. (2018)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for BMI	Derived from Locke et al. (2015)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for coronary artery disease	Derived from Nikpay et al. (2015)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for C-reactive protein	Derived from Ligthart et al. (2018)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for type 2 diabetes	Derived from Verma et al. (2024)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for glycated hemoglobin	Derived from Willems et al. (2023)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for LDL cholesterol, HDL cholesterol, Triglycerides	Derived from Graham et al. (2021)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
	PGS for bNGF, CCL11, CCL2, CCL3, CCL4, CCL7, CSF1, CSF3, CTACK, CXCL1, CXCL10, CXCL12, CXCL9, FGFb, HGF, IFNg, IL1RA, IL1b, IL10, IL13, IL16, IL17, IL18, IL2, IL2RA, IL4, IL5, IL6, IL7, IL8, IL9, MIF, PDGFbb, RANTES, SCF, SCGFb, TNFa, TNFb, TRAIL, VEGF	Derived from Konieczny et al. (2025)	Continuous	UKB (MDD and dMDD), OSR (MDD and BD)
Stress	Childhood trauma	Derived from McManus et al. (2022) based on: 20489, 20488, 20487, 20490, 20491	Continuous	UKB (MDD and dMDD)
	Adulthood stress	Derived from McManus et al. (2022) based on: 20487, 20488, 20489, 20490, 20491	Continuous	UKB (MDD and dMDD)
	Felt loved as a child	20489	Categorical with 5 levels: 0 very often, 1 often, 2 sometimes true, 3 rarely true, 4 never; reversed and one-hot encoded	UKB (MDD and dMDD)
	Physically abused by family as a child	20488	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
	Felt hated by family member as a child	20487	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
	Sexually molested as a child	20490	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)

Someone to take to doctor when needed as a child	20491	Categorical with 5 levels: 0 very often, 1 often, 2 sometimes true, 3 rarely true, 4 never; reversed and one-hot encoded	UKB (MDD and dMDD)
Been in a confiding relationship as an adult	20522	Categorical with 5 levels: 0 very often, 1 often, 2 sometimes true, 3 rarely true, 4 never; reversed and one-hot encoded	UKB (MDD and dMDD)
Physical violence by partner or ex-partner as an adult	20523	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
Belittlement by partner or ex-partner as an adult	20521	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
Sexual interference by partner or ex-partner without consent as an adult	20524	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
Able to pay rent/mortgage as an adult	20525	Categorical with 5 levels: 0 never, 1 rarely true, 2 sometimes true, 3 often, 4 very often; one-hot encoded	UKB (MDD and dMDD)
CTQ physical abuse	Derived from Bernstein et al. (2003)	Continuous	OSR (MDD and BD)
CTQ physical neglect	Derived from Bernstein et al. (2003)	Continuous	OSR (MDD and BD)
CTQ emotional abuse	Derived from Bernstein et al. (2003)	Continuous	OSR (MDD and BD)
CTQ emotional neglect	Derived from Bernstein et al. (2003)	Continuous	OSR (MDD and BD)
CTQ sexual abuse	Derived from Bernstein et al. (2003)	Continuous	OSR (MDD and BD)
SRE number of recent events	Derived from Holmes & Rahe (1967)	Continuous	OSR (MDD and BD)
SRE score of recent events	Derived from Holmes & Rahe (1967)	Continuous	OSR (MDD and BD)

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CCL, C-C motif ligand; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CTQ, Childhood Trauma Questionnaire; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; FA, fractional anisotropy; FGFB, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNG, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; OCD, obsessive-compulsive disorder; PDGFB, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; SRE, Schedule of Recent Experience; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor.

Table A2. List of antidepressant medications and their corresponding UKB code.

Antidepressant drug name	UKB Data Field
Amitriptyline	1140879616
Citalopram	1140921600
Fluoxetine	1140879540
Sertraline	1140867878
Venlafaxine	1140916282
Dosulepin	1140909806
Paroxetine	1140867888
Mirtazapine	1141152732
Escitalopram	1141180212
Trazodone	1140879634
Prozac	1140867876
Seroxat	1140882236
Ciprallex	1141190158
Duloxetine	1141200564
Lofepramine	1140867726
Clomipramine	1140879620
Nortriptyline	1140867818
Imipramine	1140879630
Dothiepin	1140879628
Cipramil	1141151946
Prothiaden	1140867624
Trimipramine	1140867756
Lustral	1140867884
Reboxetine	1141151978
Zispin	1141152736
Cymbalta	1141201834
Anafranil	1140867690
Doxepin	1140867640
Moclobemide	1140867920
Phenelzine	1140867850
Fluvoxamine	1140879544
Yentreve	1141200570
Triptafen	1140867934
Surmontil	1140867758
Tranylcypromine	1140867914
Allegron	1140867820

Edronax	1141151982
Molipaxin	1140882244
Mianserin	1140879556
Nardil	1140867852
Faverin	1140867860
Nefazodone	1140917460
Amitriptyline+Chlordiazepoxide	1140867938
Isocarboxazid	1140867856
Manerix	1140867922
Maoi	1140910820
Sinequan	1140882312
Tranlycypromine+Trifluoperazine	1140867944
Ludiomil	1140867784
Norval	1140867812
Tryptizol	1140867668
Fluphenazine Hydrochloride+Nortriptyline	1140867940
Amitriptyline Hydrochloride+Perphenazine 10mg/2mg Tablet	1140867948
Amoxapine	1140867774
Oxactin 20mg Capsule	1141174756
Efexor 37.5mg Tablet	1140916288
Prepadine 25mg Capsule	1140867628
Gamanil 70mg Tablet	1140882310
Ludiomil	1140867784
Motival	1140867930
Tofranil	1140867712
Parnate	1140867916

Table A3. Summary of consensus clustering models with dimensionally-reduced input features among the MDD sample of UKB.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	C10: 1578, C11: 2309	0.003	16.12	N.S.
DTI	4	C10: 722, C11: 475, C12: 2273, C13: 417	0.013	6.14	N.S.
rs-fMRI	2	C10: 1672, C11: 2215	0.012	8.79	N.S.
t-fMRI	3	C10: 1095, C11: 1523, C12: 1269	0.337	0.93	<0.001*
PGSs	2	C10: 1877, C11: 2010	0.017	7.41	N.S.
Stress	4	C10: 337, C11: 494, C12: 2381, C13: 675	0.396	0.94	<0.001*

Abbreviations: *Cl*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *N.S.*, not significant; *PGSs*, polygenic scores; *rs-fMRI*, resting-state *fMRI*; *Sil*, Silhouette score; *t-fMRI*, task-based *fMRI*. *Statistical significance at FDR-corrected *p*-value (i.e., *q*-value) <0.05

Table A4. Summary of consensus clustering models with dimensionally-reduced input features among the dMDD sample of UKB.

Model	Clusters	Class counts	Sil	DB	q-value
GM	4	C10: 4, C11: 12, C12: 2, C13: 261	0.049	2.92	N.S.
DTI	2	C10: 2, C11: 277	0.189	1.34	N.S.
rs-fMRI	2	C10: 21, C11: 258	0.044	4.89	N.S.
t-fMRI	5	C10: 10, C11: 31, C12: 119, C13: 54, C14: 65	0.223	1.17	<0.001*
PGSs	2	C10: 132, C11: 147	0.017	6.65	N.S.
Stress	4	C10: 52, C11: 38, C12: 157, C13: 32	0.354	1.02	<0.001*

Abbreviations: *Cl*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *N.S.*, not significant; *PGSs*, polygenic scores; *rs-fMRI*, resting-state *fMRI*; *Sil*, Silhouette score; *t-fMRI*, task-based *fMRI*. *Statistical significance at FDR-corrected *p*-value (i.e., *q*-value) <0.05

Table A5. Input feature comparisons between clusters resulting from the significant stratification models among the MDD sample of the UKB dataset.

Model	Variable	CI0	CI1	CI2	CI3	Statistic	Effect size	p-value	q-value
GM	Area of caudalanteriorcingulate L	1094.01 ± 219.79	1047.40 ± 167.23	NA	NA	2143095	0.240	<0.001	<0.001*
GM	Area of caudalanteriorcingulate R	783.75 ± 171.28	754.10 ± 153.68	NA	NA	2061107	0.183	<0.001	<0.001*
GM	Area of caudalmiddlefrontal L	2384.91 ± 363.42	2300.03 ± 334.66	NA	NA	2126554	0.243	<0.001	<0.001*
GM	Area of caudalmiddlefrontal R	2217.57 ± 350.93	2138.88 ± 331.05	NA	NA	2127349	0.231	<0.001	<0.001*
GM	Area of cuneus L	2105.45 ± 281.81	2061.88 ± 278.69	NA	NA	2053899	0.156	<0.001	<0.001*
GM	Area of cuneus R	2023.63 ± 257.68	1972.31 ± 256.58	NA	NA	2101087	0.200	<0.001	<0.001*
GM	Area of entorhinal L	424.10 ± 76.46	416.15 ± 74.48	NA	NA	2002151	0.105	<0.001	<0.001*
GM	Area of entorhinal R	376.48 ± 69.75	371.01 ± 68.12	NA	NA	1962566	0.079	0.024	0.025*
GM	Area of fusiform L	2860.27 ± 350.38	2780.06 ± 329.15	NA	NA	2127258	0.236	<0.001	<0.001*
GM	Area of fusiform R	2796.67 ± 358.49	2712.09 ± 336.69	NA	NA	2132228	0.244	<0.001	<0.001*
GM	Area of inferiorparietal L	4417.63 ± 614.45	4264.01 ± 576.97	NA	NA	2150951	0.258	<0.001	<0.001*
GM	Area of inferiorparietal R	5163.04 ± 708.05	4977.39 ± 671.33	NA	NA	2165815	0.269	<0.001	<0.001*
GM	Area of inferiortemporal L	3426.42 ± 441.03	3311.89 ± 428.31	NA	NA	2171020	0.264	<0.001	<0.001*
GM	Area of inferiortemporal R	3613.85 ± 458.21	3485.29 ± 450.74	NA	NA	2199795	0.283	<0.001	<0.001*
GM	Area of insula L	1977.56 ± 197.66	1942.31 ± 188.82	NA	NA	2071226	0.183	<0.001	<0.001*
GM	Area of insula R	2070.76 ± 205.76	2027.27 ± 196.18	NA	NA	2117077	0.217	<0.001	<0.001*
GM	Area of isthmuscingulate L	1016.04 ± 165.78	992.55 ± 152.56	NA	NA	2035632	0.148	<0.001	<0.001*
GM	Area of isthmuscingulate R	906.77 ± 143.87	882.31 ± 133.44	NA	NA	2061692	0.177	<0.001	<0.001*
GM	Area of lateraloccipital L	5058.46 ± 607.50	4934.19 ± 575.37	NA	NA	2097897	0.210	<0.001	<0.001*
GM	Area of lateraloccipital R	5152.28 ± 653.47	5008.58 ± 614.29	NA	NA	2114526	0.227	<0.001	<0.001*
GM	Area of lateralorbitofrontal L	2994.08 ± 300.49	2922.50 ± 300.31	NA	NA	2130769	0.238	<0.001	<0.001*
GM	Area of lateralorbitofrontal R	2997.80 ± 323.20	2924.31 ± 310.42	NA	NA	2125524	0.232	<0.001	<0.001*
GM	Area of lingual L	3168.26 ± 392.34	3119.47 ± 385.10	NA	NA	2009839	0.126	<0.001	<0.001*
GM	Area of lingual R	3250.18 ± 419.24	3176.30 ± 402.70	NA	NA	2076547	0.180	<0.001	<0.001*
GM	Area of medialorbitofrontal L	1603.67 ± 171.12	1566.78 ± 168.81	NA	NA	2110971	0.217	<0.001	<0.001*
GM	Area of medialorbitofrontal R	1524.02 ± 163.68	1484.60 ± 160.16	NA	NA	2147742	0.244	<0.001	<0.001*
GM	Area of middletemporal L	4200.94 ± 525.21	4056.29 ± 503.25	NA	NA	2179923	0.281	<0.001	<0.001*
GM	Area of middletemporal R	4205.06 ± 487.77	4070.59 ± 460.26	NA	NA	2193132	0.284	<0.001	<0.001*
GM	Area of paracentral L	1620.79 ± 195.20	1565.32 ± 185.58	NA	NA	2196815	0.292	<0.001	<0.001*
GM	Area of paracentral R	1603.40 ± 203.86	1545.10 ± 192.05	NA	NA	2197242	0.295	<0.001	<0.001*
GM	Area of parahippocampal L	699.60 ± 80.44	693.86 ± 80.12	NA	NA	1958925	0.072	0.031	0.032*
GM	Area of parahippocampal R	679.54 ± 78.39	671.86 ± 77.36	NA	NA	1992543	0.099	0.002	0.002*

GM	Area of parsopercularis L	1457.07 ± 215.09	1418.34 ± 204.22	NA	NA	2082840	0.185	<0.001	<0.001*
GM	Area of parsopercularis R	1552.68 ± 220.87	1495.00 ± 213.46	NA	NA	2182697	0.266	<0.001	<0.001*
GM	Area of parsorbitalis L	683.00 ± 81.81	668.34 ± 78.75	NA	NA	2074908	0.183	<0.001	<0.001*
GM	Area of parsorbitalis R	701.40 ± 98.98	684.00 ± 92.36	NA	NA	2076901	0.182	<0.001	<0.001*
GM	Area of parstriangularis L	1566.57 ± 247.01	1522.64 ± 228.66	NA	NA	2062889	0.185	<0.001	<0.001*
GM	Area of parstriangularis R	1475.42 ± 231.57	1429.49 ± 220.89	NA	NA	2106438	0.203	<0.001	<0.001*
GM	Area of pericalcarine L	1399.84 ± 243.86	1389.62 ± 241.37	NA	NA	1925904	0.042	0.228	0.228
GM	Area of pericalcarine R	1548.44 ± 262.63	1526.83 ± 255.63	NA	NA	1972855	0.083	0.011	0.011*
GM	Area of postcentral L	4656.50 ± 500.05	4503.88 ± 469.67	NA	NA	2216351	0.315	<0.001	<0.001*
GM	Area of postcentral R	4417.58 ± 511.94	4256.81 ± 482.06	NA	NA	2244332	0.324	<0.001	<0.001*
GM	Area of posteriorcingulate L	1268.86 ± 191.02	1235.59 ± 165.86	NA	NA	2061028	0.187	<0.001	<0.001*
GM	Area of posteriorcingulate R	1227.95 ± 190.72	1188.58 ± 167.82	NA	NA	2100524	0.220	<0.001	<0.001*
GM	Area of precentral L	4698.80 ± 481.93	4572.40 ± 456.66	NA	NA	2164365	0.270	<0.001	<0.001*
GM	Area of precentral R	4561.96 ± 475.29	4443.56 ± 466.73	NA	NA	2151999	0.251	<0.001	<0.001*
GM	Area of precuneus L	3751.67 ± 468.94	3604.91 ± 442.55	NA	NA	2219969	0.322	<0.001	<0.001*
GM	Area of precuneus R	4088.96 ± 506.63	3943.28 ± 487.58	NA	NA	2189082	0.293	<0.001	<0.001*
GM	Area of rostralanteriorcingulate L	1187.46 ± 198.17	1144.70 ± 190.99	NA	NA	2112052	0.220	<0.001	<0.001*
GM	Area of rostralanteriorcingulate R	819.43 ± 161.40	787.98 ± 146.91	NA	NA	2080009	0.204	<0.001	<0.001*
GM	Area of rostralmiddlefrontal L	3988.76 ± 570.59	3839.92 ± 533.43	NA	NA	2165804	0.270	<0.001	<0.001*
GM	Area of rostralmiddlefrontal R	4138.48 ± 597.68	3972.61 ± 566.43	NA	NA	2192022	0.285	<0.001	<0.001*
GM	Area of superiorfrontal L	7788.52 ± 889.40	7572.21 ± 835.50	NA	NA	2136775	0.251	<0.001	<0.001*
GM	Area of superiorfrontal R	8893.99 ± 1025.27	8649.79 ± 993.06	NA	NA	2133877	0.242	<0.001	<0.001*
GM	Area of superiorparietal L	4347.23 ± 564.26	4181.07 ± 518.81	NA	NA	2190675	0.307	<0.001	<0.001*
GM	Area of superiorparietal R	4426.52 ± 560.25	4271.65 ± 514.32	NA	NA	2177724	0.289	<0.001	<0.001*
GM	Area of superiortemporal L	5085.17 ± 549.19	4969.91 ± 519.28	NA	NA	2108636	0.216	<0.001	<0.001*
GM	Area of superiortemporal R	4757.35 ± 468.11	4650.38 ± 441.98	NA	NA	2131782	0.235	<0.001	<0.001*
GM	Area of supramarginal L	3650.45 ± 582.48	3516.39 ± 540.14	NA	NA	2131758	0.239	<0.001	<0.001*
GM	Area of supramarginal R	3438.13 ± 495.24	3336.08 ± 455.02	NA	NA	2109197	0.215	<0.001	<0.001*
GM	Area of transversetemporal L	454.18 ± 72.44	440.73 ± 67.36	NA	NA	2089185	0.193	<0.001	<0.001*
GM	Area of transversetemporal R	333.89 ± 47.57	321.17 ± 44.53	NA	NA	2164592	0.276	<0.001	<0.001*
GM	Volume of caudalanteriorcingulate L	3132.15 ± 597.93	3151.45 ± 567.78	NA	NA	1836771	-0.033	0.179	0.180
GM	Volume of caudalanteriorcingulate R	2245.39 ± 578.14	2300.67 ± 553.98	NA	NA	1775760	-0.098	0.002	0.002*
GM	Volume of caudalmiddlefrontal L	7098.36 ± 1134.38	7324.41 ± 1119.64	NA	NA	1662985	-0.201	<0.001	<0.001*
GM	Volume of caudalmiddlefrontal R	6573.50 ± 1099.75	6762.70 ± 1113.61	NA	NA	1695737	-0.171	<0.001	<0.001*
GM	Volume of cuneus L	4243.27 ± 669.06	4525.75 ± 706.30	NA	NA	1445327	-0.410	<0.001	<0.001*

GM	Volume of cuneus R	3824.65 ± 589.32	4071.00 ± 654.19	NA	NA	1469095	-0.395	<0.001	<0.001*
GM	Volume of entorhinal L	1742.47 ± 335.68	1814.61 ± 343.05	NA	NA	1649416	-0.212	<0.001	<0.001*
GM	Volume of entorhinal R	1649.99 ± 317.36	1742.39 ± 326.95	NA	NA	1578593	-0.287	<0.001	<0.001*
GM	Volume of fusiform L	9051.65 ± 1201.12	9325.47 ± 1202.48	NA	NA	1637135	-0.228	<0.001	<0.001*
GM	Volume of fusiform R	8780.62 ± 1230.65	9123.01 ± 1244.45	NA	NA	1578313	-0.277	<0.001	<0.001*
GM	Volume of inferiorparietal L	12552.28 ± 1788.70	12912.53 ± 1765.87	NA	NA	1661144	-0.203	<0.001	<0.001*
GM	Volume of inferiorparietal R	14899.55 ± 2056.18	15417.93 ± 2091.77	NA	NA	1626908	-0.250	<0.001	<0.001*
GM	Volume of inferiortemporal L	12414.57 ± 1662.76	12726.11 ± 1657.88	NA	NA	1681016	-0.188	<0.001	<0.001*
GM	Volume of inferiortemporal R	12564.96 ± 1660.07	12931.55 ± 1715.92	NA	NA	1652377	-0.217	<0.001	<0.001*
GM	Volume of insula L	6236.74 ± 652.73	6435.68 ± 656.30	NA	NA	1549200	-0.304	<0.001	<0.001*
GM	Volume of insula R	6450.15 ± 680.32	6668.78 ± 681.71	NA	NA	1538423	-0.321	<0.001	<0.001*
GM	Volume of isthmuscingulate L	2680.59 ± 438.97	2764.23 ± 435.08	NA	NA	1681087	-0.191	<0.001	<0.001*
GM	Volume of isthmuscingulate R	2546.72 ± 410.74	2621.71 ± 411.11	NA	NA	1678926	-0.182	<0.001	<0.001*
GM	Volume of lateraloccipital L	12267.35 ± 1649.47	12912.27 ± 1655.13	NA	NA	1469159	-0.390	<0.001	<0.001*
GM	Volume of lateraloccipital R	12535.08 ± 1755.57	13247.20 ± 1779.45	NA	NA	1453312	-0.403	<0.001	<0.001*
GM	Volume of lateralorbitofrontal L	9094.45 ± 953.37	9384.17 ± 978.92	NA	NA	1569279	-0.300	<0.001	<0.001*
GM	Volume of lateralorbitofrontal R	9052.21 ± 940.73	9376.67 ± 947.55	NA	NA	1514711	-0.344	<0.001	<0.001*
GM	Volume of lingual L	6463.92 ± 1067.86	6866.93 ± 1104.84	NA	NA	1484655	-0.371	<0.001	<0.001*
GM	Volume of lingual R	6452.24 ± 1061.53	6848.69 ± 1090.86	NA	NA	1488022	-0.368	<0.001	<0.001*
GM	Volume of medialorbitofrontal L	4983.13 ± 573.65	5128.84 ± 585.08	NA	NA	1627641	-0.251	<0.001	<0.001*
GM	Volume of medialorbitofrontal R	4830.61 ± 540.51	4992.87 ± 553.76	NA	NA	1562038	-0.296	<0.001	<0.001*
GM	Volume of middletemporal L	14006.78 ± 1887.90	14401.42 ± 1881.49	NA	NA	1656054	-0.209	<0.001	<0.001*
GM	Volume of middletemporal R	14180.85 ± 1782.14	14632.07 ± 1767.62	NA	NA	1619194	-0.254	<0.001	<0.001*
GM	Volume of paracentral L	4537.41 ± 566.89	4789.16 ± 577.77	NA	NA	1411518	-0.440	<0.001	<0.001*
GM	Volume of paracentral R	4388.95 ± 596.45	4632.55 ± 601.79	NA	NA	1445665	-0.406	<0.001	<0.001*
GM	Volume of parahippocampal L	2125.00 ± 307.45	2260.09 ± 316.74	NA	NA	1416219	-0.432	<0.001	<0.001*
GM	Volume of parahippocampal R	2009.49 ± 261.09	2133.08 ± 268.07	NA	NA	1392354	-0.467	<0.001	<0.001*
GM	Volume of parsopercularis L	4524.97 ± 700.31	4680.60 ± 709.08	NA	NA	1634082	-0.221	<0.001	<0.001*
GM	Volume of parsopercularis R	4666.49 ± 700.64	4780.04 ± 727.38	NA	NA	1721119	-0.159	<0.001	<0.001*
GM	Volume of parsorbitalis L	2243.36 ± 306.91	2336.93 ± 309.07	NA	NA	1552502	-0.304	<0.001	<0.001*
GM	Volume of parsorbitalis R	2303.65 ± 342.07	2407.34 ± 344.75	NA	NA	1558873	-0.302	<0.001	<0.001*
GM	Volume of parstriangularis L	4501.68 ± 764.78	4655.29 ± 739.43	NA	NA	1633627	-0.204	<0.001	<0.001*
GM	Volume of parstriangularis R	4162.67 ± 691.70	4298.37 ± 721.40	NA	NA	1684324	-0.192	<0.001	<0.001*
GM	Volume of pericalcarine L	2051.08 ± 412.96	2172.97 ± 440.32	NA	NA	1579221	-0.285	<0.001	<0.001*
GM	Volume of pericalcarine R	2221.62 ± 425.24	2349.82 ± 465.82	NA	NA	1595040	-0.287	<0.001	<0.001*

GM	Volume of postcentral L	11500.98 ± 1442.13	12013.03 ± 1446.78	NA	NA	1504458	-0.354	<0.001	<0.001*
GM	Volume of postcentral R	10734.67 ± 1429.44	11191.36 ± 1441.29	NA	NA	1547883	-0.318	<0.001	<0.001*
GM	Volume of posteriorcingulate L	3571.91 ± 533.35	3650.27 ± 515.64	NA	NA	1717149	-0.149	<0.001	<0.001*
GM	Volume of posteriorcingulate R	3616.99 ± 536.80	3699.89 ± 530.98	NA	NA	1701729	-0.155	<0.001	<0.001*
GM	Volume of precentral L	13767.77 ± 1594.63	14534.75 ± 1589.34	NA	NA	1367678	-0.482	<0.001	<0.001*
GM	Volume of precentral R	13211.04 ± 1533.29	14011.25 ± 1579.24	NA	NA	1338481	-0.514	<0.001	<0.001*
GM	Volume of precuneus L	10313.96 ± 1273.57	10657.80 ± 1276.99	NA	NA	1592420	-0.270	<0.001	<0.001*
GM	Volume of precuneus R	10980.38 ± 1335.14	11402.04 ± 1366.14	NA	NA	1548975	-0.312	<0.001	<0.001*
GM	Volume of rostralanteriorcingulate L	3731.07 ± 615.06	3786.73 ± 632.73	NA	NA	1785451	-0.089	0.005	0.005*
GM	Volume of rostralanteriorcingulate R	2666.90 ± 539.57	2703.94 ± 517.86	NA	NA	1787933	-0.070	0.006	0.006*
GM	Volume of rostralmiddlefrontal L	11571.55 ± 1688.05	11890.01 ± 1674.22	NA	NA	1686938	-0.189	<0.001	<0.001*
GM	Volume of rostralmiddlefrontal R	11724.39 ± 1753.07	11965.38 ± 1753.99	NA	NA	1739745	-0.137	<0.001	<0.001*
GM	Volume of superiorfrontal L	25227.76 ± 2846.97	26190.75 ± 2865.59	NA	NA	1517405	-0.337	<0.001	<0.001*
GM	Volume of superiorfrontal R	28071.58 ± 3206.05	29096.76 ± 3372.37	NA	NA	1551416	-0.311	<0.001	<0.001*
GM	Volume of superiorparietal L	11436.86 ± 1552.16	11767.25 ± 1522.63	NA	NA	1652440	-0.215	<0.001	<0.001*
GM	Volume of superiorparietal R	11488.04 ± 1557.23	11941.89 ± 1513.04	NA	NA	1553813	-0.296	<0.001	<0.001*
GM	Volume of superiortemporal L	16989.67 ± 1914.46	17802.85 ± 1914.33	NA	NA	1427699	-0.425	<0.001	<0.001*
GM	Volume of superiortemporal R	16145.49 ± 1676.05	16897.20 ± 1670.11	NA	NA	1409016	-0.449	<0.001	<0.001*
GM	Volume of supramarginal L	10767.63 ± 1699.93	11089.10 ± 1682.76	NA	NA	1671294	-0.190	<0.001	<0.001*
GM	Volume of supramarginal R	10121.52 ± 1468.15	10517.46 ± 1446.80	NA	NA	1583903	-0.272	<0.001	<0.001*
GM	Volume of transversetemporal L	1210.26 ± 225.72	1281.65 ± 226.62	NA	NA	1539238	-0.316	<0.001	<0.001*
GM	Volume of transversetemporal R	958.02 ± 169.27	1023.63 ± 169.70	NA	NA	1456379	-0.387	<0.001	<0.001*
GM	Mean thickness of caudalanteriorcingulate L	2.68 ± 0.27	2.82 ± 0.26	NA	NA	1340200	-0.501	<0.001	<0.001*
GM	Mean thickness of caudalanteriorcingulate R	2.47 ± 0.33	2.61 ± 0.31	NA	NA	1413167	-0.439	<0.001	<0.001*
GM	Mean thickness of caudalmiddlefrontal L	2.80 ± 0.12	2.96 ± 0.11	NA	NA	655012	-1.328	<0.001	<0.001*
GM	Mean thickness of caudalmiddlefrontal R	2.76 ± 0.12	2.91 ± 0.11	NA	NA	697257	-1.272	<0.001	<0.001*
GM	Mean thickness of cuneus L	1.98 ± 0.12	2.12 ± 0.13	NA	NA	830331.5	-1.095	<0.001	<0.001*
GM	Mean thickness of cuneus R	1.88 ± 0.12	2.02 ± 0.13	NA	NA	849161.5	-1.065	<0.001	<0.001*
GM	Mean thickness of entorhinal L	3.18 ± 0.29	3.34 ± 0.26	NA	NA	1314851	-0.552	<0.001	<0.001*
GM	Mean thickness of entorhinal R	3.26 ± 0.31	3.43 ± 0.29	NA	NA	1304703	-0.558	<0.001	<0.001*
GM	Mean thickness of fusiform L	2.83 ± 0.11	2.96 ± 0.10	NA	NA	748733.5	-1.200	<0.001	<0.001*
GM	Mean thickness of fusiform R	2.81 ± 0.12	2.96 ± 0.11	NA	NA	683334.5	-1.274	<0.001	<0.001*
GM	Mean thickness of inferioparietal L	2.65 ± 0.10	2.78 ± 0.09	NA	NA	576984	-1.429	<0.001	<0.001*
GM	Mean thickness of inferioparietal R	2.67 ± 0.10	2.82 ± 0.09	NA	NA	499556.5	-1.551	<0.001	<0.001*
GM	Mean thickness of inferiortemporal L	2.99 ± 0.12	3.12 ± 0.12	NA	NA	837131	-1.075	<0.001	<0.001*

GM	Mean thickness of inferiortemporal R	2.95 ± 0.11	3.09 ± 0.12	NA	NA	736660	-1.203	<0.001	<0.001*
GM	Mean thickness of insula L	3.14 ± 0.15	3.27 ± 0.14	NA	NA	953186.5	-0.925	<0.001	<0.001*
GM	Mean thickness of insula R	3.12 ± 0.14	3.27 ± 0.13	NA	NA	855171.5	-1.057	<0.001	<0.001*
GM	Mean thickness of isthmuscingulate L	2.43 ± 0.17	2.53 ± 0.17	NA	NA	1235767	-0.610	<0.001	<0.001*
GM	Mean thickness of isthmuscingulate R	2.49 ± 0.18	2.60 ± 0.19	NA	NA	1238246	-0.614	<0.001	<0.001*
GM	Mean thickness of lateraloccipital L	2.26 ± 0.11	2.39 ± 0.11	NA	NA	698201.5	-1.263	<0.001	<0.001*
GM	Mean thickness of lateraloccipital R	2.28 ± 0.11	2.43 ± 0.11	NA	NA	648786	-1.323	<0.001	<0.001*
GM	Mean thickness of lateralorbitofrontal L	2.77 ± 0.12	2.90 ± 0.12	NA	NA	859237	-1.051	<0.001	<0.001*
GM	Mean thickness of lateralorbitofrontal R	2.76 ± 0.12	2.89 ± 0.12	NA	NA	-33.939	-1.090	<0.001	<0.001*
GM	Mean thickness of lingual L	1.97 ± 0.13	2.09 ± 0.14	NA	NA	-27.6952	-0.889	<0.001	<0.001*
GM	Mean thickness of lingual R	1.95 ± 0.13	2.07 ± 0.14	NA	NA	948818.5	-0.940	<0.001	<0.001*
GM	Mean thickness of medialorbitofrontal L	2.60 ± 0.16	2.71 ± 0.15	NA	NA	1143135	-0.713	<0.001	<0.001*
GM	Mean thickness of medialorbitofrontal R	2.62 ± 0.17	2.75 ± 0.16	NA	NA	1122978	-0.737	<0.001	<0.001*
GM	Mean thickness of middletemporal L	2.84 ± 0.13	2.99 ± 0.12	NA	NA	781598	-1.127	<0.001	<0.001*
GM	Mean thickness of middletemporal R	2.91 ± 0.12	3.07 ± 0.12	NA	NA	693892	-1.270	<0.001	<0.001*
GM	Mean thickness of paracentral L	2.62 ± 0.16	2.82 ± 0.15	NA	NA	691749.5	-1.254	<0.001	<0.001*
GM	Mean thickness of paracentral R	2.60 ± 0.16	2.80 ± 0.15	NA	NA	672549.5	-1.295	<0.001	<0.001*
GM	Mean thickness of parahippocampal L	2.71 ± 0.29	2.87 ± 0.28	NA	NA	1303272	-0.555	<0.001	<0.001*
GM	Mean thickness of parahippocampal R	2.64 ± 0.24	2.80 ± 0.23	NA	NA	1206887	-0.665	<0.001	<0.001*
GM	Mean thickness of parsopercularis L	2.81 ± 0.13	2.95 ± 0.12	NA	NA	799072	-1.127	<0.001	<0.001*
GM	Mean thickness of parsopercularis R	2.77 ± 0.12	2.90 ± 0.12	NA	NA	771640.5	-1.170	<0.001	<0.001*
GM	Mean thickness of parsorbitalis L	2.82 ± 0.15	2.96 ± 0.15	NA	NA	-28.8165	-0.925	<0.001	<0.001*
GM	Mean thickness of parsorbitalis R	2.82 ± 0.16	2.97 ± 0.16	NA	NA	932659	-0.945	<0.001	<0.001*
GM	Mean thickness of parstriangularis L	2.65 ± 0.12	2.78 ± 0.11	NA	NA	801238.5	-1.129	<0.001	<0.001*
GM	Mean thickness of parstriangularis R	2.63 ± 0.11	2.76 ± 0.11	NA	NA	-36.3704	-1.168	<0.001	<0.001*
GM	Mean thickness of pericalcarine L	1.69 ± 0.13	1.79 ± 0.14	NA	NA	1077242	-0.798	<0.001	<0.001*
GM	Mean thickness of pericalcarine R	1.64 ± 0.13	1.76 ± 0.14	NA	NA	1039768	-0.836	<0.001	<0.001*
GM	Mean thickness of postcentral L	2.29 ± 0.11	2.44 ± 0.11	NA	NA	664214	-1.302	<0.001	<0.001*
GM	Mean thickness of postcentral R	2.24 ± 0.12	2.39 ± 0.12	NA	NA	725872.5	-1.189	<0.001	<0.001*
GM	Mean thickness of posteriorcingulate L	2.64 ± 0.16	2.74 ± 0.16	NA	NA	1238676	-0.631	<0.001	<0.001*
GM	Mean thickness of posteriorcingulate R	2.65 ± 0.16	2.76 ± 0.16	NA	NA	1190597	-0.675	<0.001	<0.001*
GM	Mean thickness of precentral L	2.75 ± 0.14	2.95 ± 0.12	NA	NA	532519.5	-1.460	<0.001	<0.001*
GM	Mean thickness of precentral R	2.70 ± 0.14	2.90 ± 0.13	NA	NA	519276	-1.452	<0.001	<0.001*
GM	Mean thickness of precuneus L	2.57 ± 0.11	2.72 ± 0.10	NA	NA	639502	-1.347	<0.001	<0.001*
GM	Mean thickness of precuneus R	2.56 ± 0.10	2.71 ± 0.10	NA	NA	543901	-1.492	<0.001	<0.001*

GM	Mean thickness of rostralanteriorcingulate L	2.84 ± 0.17	2.96 ± 0.17	NA	NA	1116364	-0.746	<0.001	<0.001*
GM	Mean thickness of rostralanteriorcingulate R	2.88 ± 0.19	3.01 ± 0.18	NA	NA	1163220	-0.694	<0.001	<0.001*
GM	Mean thickness of rostralmiddlefrontal L	2.63 ± 0.10	2.76 ± 0.10	NA	NA	628090.5	-1.359	<0.001	<0.001*
GM	Mean thickness of rostralmiddlefrontal R	2.58 ± 0.09	2.70 ± 0.09	NA	NA	609922.5	-1.375	<0.001	<0.001*
GM	Mean thickness of superiorfrontal L	2.89 ± 0.11	3.04 ± 0.10	NA	NA	576649	-1.436	<0.001	<0.001*
GM	Mean thickness of superiorfrontal R	2.85 ± 0.10	3.00 ± 0.09	NA	NA	520440	-1.526	<0.001	<0.001*
GM	Mean thickness of superiorparietal L	2.43 ± 0.10	2.56 ± 0.10	NA	NA	612778	-1.375	<0.001	<0.001*
GM	Mean thickness of superiorparietal R	2.40 ± 0.10	2.54 ± 0.10	NA	NA	591384	-1.409	<0.001	<0.001*
GM	Mean thickness of superiortemporal L	2.91 ± 0.14	3.08 ± 0.13	NA	NA	689894	-1.267	<0.001	<0.001*
GM	Mean thickness of superiortemporal R	2.99 ± 0.13	3.16 ± 0.12	NA	NA	627049.5	-1.358	<0.001	<0.001*
GM	Mean thickness of supramarginal L	2.76 ± 0.11	2.91 ± 0.10	NA	NA	602761.5	-1.395	<0.001	<0.001*
GM	Mean thickness of supramarginal R	2.76 ± 0.11	2.92 ± 0.11	NA	NA	572362	-1.440	<0.001	<0.001*
GM	Mean thickness of transversetemporal L	2.45 ± 0.23	2.65 ± 0.23	NA	NA	-26.7866	-0.860	<0.001	<0.001*
GM	Mean thickness of transversetemporal R	2.49 ± 0.24	2.71 ± 0.24	NA	NA	959276.5	-0.922	<0.001	<0.001*
GM	Volume of accumbens L	517.25 ± 112.05	528.34 ± 115.78	NA	NA	1766343	-0.097	<0.001	<0.001*
GM	Volume of accumbens R	413.15 ± 101.50	423.00 ± 103.92	NA	NA	1781240	-0.096	0.003	0.004*
GM	Volume of amygdala L	1232.51 ± 246.23	1259.95 ± 244.26	NA	NA	1747303	-0.112	<0.001	<0.001*
GM	Volume of amygdala R	1192.70 ± 267.81	1225.95 ± 271.43	NA	NA	1765811	-0.123	<0.001	<0.001*
GM	Volume of caudate L	3351.12 ± 396.00	3413.56 ± 405.40	NA	NA	1724629	-0.156	<0.001	<0.001*
GM	Volume of caudate R	3516.25 ± 416.87	3585.18 ± 424.10	NA	NA	1709525	-0.164	<0.001	<0.001*
GM	Volume of hippocampus L	3817.40 ± 447.65	3879.77 ± 470.21	NA	NA	1733099	-0.136	<0.001	<0.001*
GM	Volume of hippocampus R	3930.82 ± 460.37	3989.22 ± 455.19	NA	NA	1762147	-0.128	<0.001	<0.001*
GM	Volume of pallidum L	1738.72 ± 232.35	1762.30 ± 229.95	NA	NA	1767460	-0.102	<0.001	<0.001*
GM	Volume of pallidum R	1798.88 ± 232.29	1809.66 ± 227.48	NA	NA	1833129	-0.047	0.147	0.149
GM	Volume of putamen L	4829.06 ± 547.43	4865.56 ± 568.51	NA	NA	1827002	-0.065	0.104	0.106
GM	Volume of putamen R	4862.53 ± 547.06	4904.65 ± 569.40	NA	NA	1814013	-0.075	0.046	0.047*
GM	Volume of thalamus L	7809.88 ± 744.63	7879.75 ± 746.72	NA	NA	1774740	-0.094	0.002	0.002*
GM	Volume of thalamus R	7604.66 ± 728.69	7686.34 ± 731.55	NA	NA	1751444	-0.112	<0.001	<0.001*
DTI	Mean FA in anterior corona radiata L	0.45 ± 0.02	0.48 ± 0.02	NA	NA	662958	-1.315	<0.001	<0.001*
DTI	Mean FA in anterior corona radiata R	0.45 ± 0.02	0.48 ± 0.02	NA	NA	702352.5	-1.263	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule L	0.58 ± 0.02	0.60 ± 0.02	NA	NA	811815.5	-1.092	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule R	0.59 ± 0.02	0.61 ± 0.02	NA	NA	834648.5	-1.069	<0.001	<0.001*
DTI	Mean FA in body of corpus callosum	0.70 ± 0.02	0.73 ± 0.02	NA	NA	573408.5	-1.411	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle L	0.71 ± 0.02	0.73 ± 0.02	NA	NA	982386	-0.881	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle R	0.70 ± 0.02	0.72 ± 0.02	NA	NA	919647.5	-0.960	<0.001	<0.001*

DTI	Mean FA in cingulum cingulate gyrus L	0.61 ± 0.03	0.64 ± 0.03	NA	NA	823900.5	-1.076	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus R	0.57 ± 0.03	0.60 ± 0.03	NA	NA	851103.5	-1.055	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus L	0.45 ± 0.03	0.47 ± 0.03	NA	NA	1162511	-0.679	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus R	0.45 ± 0.03	0.47 ± 0.03	NA	NA	1207542	-0.643	<0.001	<0.001*
DTI	Mean FA in corticospinal tract L	0.53 ± 0.03	0.55 ± 0.03	NA	NA	1267406	-0.578	<0.001	<0.001*
DTI	Mean FA in corticospinal tract R	0.51 ± 0.04	0.53 ± 0.03	NA	NA	1343188	-0.505	<0.001	<0.001*
DTI	Mean FA in external capsule L	0.46 ± 0.02	0.48 ± 0.02	NA	NA	884235	-1.017	<0.001	<0.001*
DTI	Mean FA in external capsule R	0.45 ± 0.02	0.47 ± 0.02	NA	NA	838476	-1.069	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis L	0.52 ± 0.03	0.55 ± 0.03	NA	NA	1109838	-0.741	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis R	0.52 ± 0.03	0.55 ± 0.03	NA	NA	1079948	-0.779	<0.001	<0.001*
DTI	Mean FA in fornix	0.46 ± 0.08	0.48 ± 0.07	NA	NA	1505487	-0.351	<0.001	<0.001*
DTI	Mean FA in genu of corpus callosum	0.71 ± 0.03	0.75 ± 0.02	NA	NA	562849	-1.411	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle L	0.54 ± 0.03	0.56 ± 0.03	NA	NA	1081332	-0.736	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle R	0.55 ± 0.03	0.56 ± 0.02	NA	NA	1081809	-0.751	<0.001	<0.001*
DTI	Mean FA in medial lemniscus L	0.58 ± 0.03	0.60 ± 0.02	NA	NA	1116722	-0.744	<0.001	<0.001*
DTI	Mean FA in medial lemniscus R	0.59 ± 0.03	0.60 ± 0.02	NA	NA	1100943	-0.751	<0.001	<0.001*
DTI	Mean FA in middle cerebellar peduncle	0.54 ± 0.02	0.55 ± 0.02	NA	NA	1078955	-0.784	<0.001	<0.001*
DTI	Mean FA in pontine crossing tract	0.40 ± 0.03	0.41 ± 0.03	NA	NA	1458613	-0.387	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata L	0.47 ± 0.02	0.50 ± 0.02	NA	NA	553425.5	-1.431	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata R	0.48 ± 0.02	0.51 ± 0.02	NA	NA	603526.5	-1.364	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule L	0.68 ± 0.02	0.70 ± 0.02	NA	NA	1064546	-0.797	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule R	0.67 ± 0.02	0.69 ± 0.02	NA	NA	1061122	-0.803	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation L	0.59 ± 0.03	0.63 ± 0.02	NA	NA	639668.5	-1.312	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation R	0.58 ± 0.03	0.62 ± 0.02	NA	NA	627197	-1.344	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule L	0.60 ± 0.02	0.63 ± 0.02	NA	NA	906804.5	-0.981	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule R	0.58 ± 0.03	0.61 ± 0.02	NA	NA	930815	-0.960	<0.001	<0.001*
DTI	Mean FA in sagittal stratum L	0.55 ± 0.03	0.58 ± 0.03	NA	NA	818271	-1.082	<0.001	<0.001*
DTI	Mean FA in sagittal stratum R	0.55 ± 0.03	0.58 ± 0.02	NA	NA	676831	-1.279	<0.001	<0.001*
DTI	Mean FA in splenium of corpus callosum	0.78 ± 0.02	0.80 ± 0.02	NA	NA	761973	-1.109	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle L	0.70 ± 0.02	0.71 ± 0.02	NA	NA	1067093	-0.772	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle R	0.69 ± 0.02	0.70 ± 0.02	NA	NA	1072809	-0.759	<0.001	<0.001*
DTI	Mean FA in superior corona radiata L	0.48 ± 0.02	0.51 ± 0.02	NA	NA	673055.5	-1.280	<0.001	<0.001*
DTI	Mean FA in superior corona radiata R	0.47 ± 0.02	0.50 ± 0.02	NA	NA	746375	-1.183	<0.001	<0.001*

DTI	Mean FA in superior fronto-occipital fasciculus L	0.46 ± 0.04	0.48 ± 0.03	NA	NA	1036622	-0.838	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus R	0.45 ± 0.04	0.48 ± 0.03	NA	NA	1138413	-0.724	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus L	0.52 ± 0.02	0.54 ± 0.02	NA	NA	642977	-1.321	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus R	0.51 ± 0.02	0.54 ± 0.02	NA	NA	619020.5	-1.351	<0.001	<0.001*
DTI	Mean FA in tapetum L	0.57 ± 0.06	0.60 ± 0.06	NA	NA	1321287	-0.516	<0.001	<0.001*
DTI	Mean FA in tapetum R	0.54 ± 0.06	0.58 ± 0.06	NA	NA	1243113	-0.614	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus L	0.50 ± 0.04	0.52 ± 0.03	NA	NA	1201494	-0.652	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus R	0.51 ± 0.03	0.54 ± 0.03	NA	NA	1191877	-0.670	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2743157	0.902	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2684040	0.838	<0.001	<0.001*
DTI	Mean AD in anterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	NA	NA	2212493	0.349	<0.001	<0.001*
DTI	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	NA	NA	2178371	0.314	<0.001	<0.001*
DTI	Mean AD in body of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	NA	NA	2378381	0.487	<0.001	<0.001*
DTI	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	1867618	0.000	0.862	0.862
DTI	Mean AD in cerebral peduncle R	0.15 ± 0.01	0.14 ± 0.01	NA	NA	2008921	0.125	<0.001	<0.001*
DTI	Mean AD in cingulum cingulate gyrus L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	2063634	0.173	<0.001	<0.001*
DTI	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	NA	NA	2066957	0.190	<0.001	<0.001*
DTI	Mean AD in cingulum hippocampus L	0.12 ± 0.01	0.12 ± 0.01	NA	NA	2205262	0.327	<0.001	<0.001*
DTI	Mean AD in cingulum hippocampus R	0.12 ± 0.01	0.12 ± 0.01	NA	NA	10.52431	0.340	<0.001	<0.001*
DTI	Mean AD in corticospinal tract L	0.13 ± 0.01	0.13 ± 0.01	NA	NA	2037003	0.165	<0.001	<0.001*
DTI	Mean AD in corticospinal tract R	0.13 ± 0.01	0.13 ± 0.01	NA	NA	2002166	0.137	<0.001	<0.001*
DTI	Mean AD in external capsule L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2427911	0.548	<0.001	<0.001*
DTI	Mean AD in external capsule R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2500859	0.617	<0.001	<0.001*
DTI	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	2243159	0.366	<0.001	<0.001*
DTI	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	NA	NA	2335814	0.466	<0.001	<0.001*
DTI	Mean AD in fornix	0.22 ± 0.02	0.22 ± 0.02	NA	NA	2065854	0.208	<0.001	<0.001*
DTI	Mean AD in genu of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	NA	NA	2459084	0.579	<0.001	<0.001*
DTI	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2039945	0.169	<0.001	<0.001*
DTI	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2007621	0.133	<0.001	<0.001*
DTI	Mean AD in medial lemniscus L	0.14 ± 0.01	0.13 ± 0.01	NA	NA	1972928	0.102	0.001	0.001*
DTI	Mean AD in medial lemniscus R	0.14 ± 0.01	0.13 ± 0.01	NA	NA	1942826	0.082	0.019	0.019*
DTI	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	NA	NA	8.633025	0.279	<0.001	<0.001*
DTI	Mean AD in pontine crossing tract	0.12 ± 0.01	0.11 ± 0.01	NA	NA	2082217	0.198	<0.001	<0.001*
DTI	Mean AD in posterior corona radiata L	0.13 ± 0.01	0.12 ± 0.00	NA	NA	2757230	0.896	<0.001	<0.001*

DTI	Mean AD in posterior corona radiata R	0.13 ± 0.01	0.13 ± 0.00	NA	NA	2726134	0.872	<0.001	<0.001*
DTI	Mean AD in posterior limb of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	NA	NA	2021101	0.166	<0.001	<0.001*
DTI	Mean AD in posterior limb of internal capsule R	0.14 ± 0.00	0.14 ± 0.00	NA	NA	2099451	0.239	<0.001	<0.001*
DTI	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	NA	NA	2466826	0.582	<0.001	<0.001*
DTI	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.00	NA	NA	2448814	0.567	<0.001	<0.001*
DTI	Mean AD in retrolenticular part of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	NA	NA	2343619	0.459	<0.001	<0.001*
DTI	Mean AD in retrolenticular part of internal capsule R	0.14 ± 0.00	0.13 ± 0.00	NA	NA	2457725	0.586	<0.001	<0.001*
DTI	Mean AD in sagittal stratum L	0.14 ± 0.01	0.13 ± 0.00	NA	NA	2490700	0.608	<0.001	<0.001*
DTI	Mean AD in sagittal stratum R	0.14 ± 0.01	0.14 ± 0.00	NA	NA	2522519	0.654	<0.001	<0.001*
DTI	Mean AD in splenium of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	NA	NA	2315889	0.439	<0.001	<0.001*
DTI	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	NA	NA	2049924	0.167	<0.001	<0.001*
DTI	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	NA	NA	6.330374	0.205	<0.001	<0.001*
DTI	Mean AD in superior corona radiata L	0.12 ± 0.00	0.11 ± 0.00	NA	NA	2496288	0.637	<0.001	<0.001*
DTI	Mean AD in superior corona radiata R	0.12 ± 0.00	0.11 ± 0.00	NA	NA	2499292	0.647	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus L	0.12 ± 0.01	0.11 ± 0.01	NA	NA	2393696	0.529	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus R	0.12 ± 0.01	0.11 ± 0.01	NA	NA	2304278	0.442	<0.001	<0.001*
DTI	Mean AD in superior longitudinal fasciculus L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2565679	0.704	<0.001	<0.001*
DTI	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	2598818	0.733	<0.001	<0.001*
DTI	Mean AD in tapetum L	0.17 ± 0.02	0.16 ± 0.01	NA	NA	2233286	0.372	<0.001	<0.001*
DTI	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	NA	NA	2264598	0.398	<0.001	<0.001*
DTI	Mean AD in uncinate fasciculus L	0.12 ± 0.01	0.12 ± 0.01	NA	NA	2059951	0.178	<0.001	<0.001*
DTI	Mean AD in uncinate fasciculus R	0.12 ± 0.01	0.12 ± 0.01	NA	NA	2061776	0.188	<0.001	<0.001*
DTI	Mean RD in anterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3342848	1.708	<0.001	<0.001*
DTI	Mean RD in anterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3324271	1.702	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	3011000	1.166	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	2995446	1.126	<0.001	<0.001*
DTI	Mean RD in body of corpus callosum	0.04 ± 0.00	0.04 ± 0.00	NA	NA	3252606	1.549	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle L	0.04 ± 0.00	0.03 ± 0.00	NA	NA	2738649	0.865	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle R	0.04 ± 0.00	0.03 ± 0.00	NA	NA	2840737	0.989	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.04 ± 0.00	NA	NA	3151652	1.423	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.04 ± 0.00	NA	NA	3152923	1.432	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.05 ± 0.00	NA	NA	2857266	0.978	<0.001	<0.001*

DTI	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.05 ± 0.00	NA	NA	2837859	0.992	<0.001	<0.001*
DTI	Mean RD in corticospinal tract L	0.05 ± 0.01	0.05 ± 0.01	NA	NA	2369440	0.473	<0.001	<0.001*
DTI	Mean RD in corticospinal tract R	0.06 ± 0.01	0.05 ± 0.01	NA	NA	2276441	0.383	<0.001	<0.001*
DTI	Mean RD in external capsule L	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3001248	1.204	<0.001	<0.001*
DTI	Mean RD in external capsule R	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3058132	1.267	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis L	0.06 ± 0.01	0.05 ± 0.00	NA	NA	2733473	0.800	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.01	0.06 ± 0.00	NA	NA	2788432	0.875	<0.001	<0.001*
DTI	Mean RD in fornix	0.11 ± 0.03	0.10 ± 0.03	NA	NA	2148406	0.271	<0.001	<0.001*
DTI	Mean RD in genu of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	NA	NA	3212869	1.465	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2822657	0.891	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2816003	0.946	<0.001	<0.001*
DTI	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2532212	0.598	<0.001	<0.001*
DTI	Mean RD in medial lemniscus R	0.05 ± 0.00	0.04 ± 0.00	NA	NA	2532915	0.597	<0.001	<0.001*
DTI	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2695456	0.821	<0.001	<0.001*
DTI	Mean RD in pontine crossing tract	0.06 ± 0.01	0.06 ± 0.01	NA	NA	2190161	0.329	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3375443	1.587	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	NA	NA	3331472	1.578	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	2831842	0.995	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	2850691	1.014	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3212861	1.405	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3253548	1.539	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.00	0.04 ± 0.00	NA	NA	3056714	1.228	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3068471	1.247	<0.001	<0.001*
DTI	Mean RD in sagittal stratum L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3149624	1.412	<0.001	<0.001*
DTI	Mean RD in sagittal stratum R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3261545	1.565	<0.001	<0.001*
DTI	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.03 ± 0.00	NA	NA	3129944	1.301	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	2661582	0.742	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	2661441	0.768	<0.001	<0.001*
DTI	Mean RD in superior corona radiata L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3386005	1.773	<0.001	<0.001*
DTI	Mean RD in superior corona radiata R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3341834	1.691	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.01	0.05 ± 0.00	NA	NA	2922742	0.867	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.01	0.05 ± 0.00	NA	NA	2891759	0.924	<0.001	<0.001*
DTI	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3331881	1.668	<0.001	<0.001*

DTI	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	3352147	1.702	<0.001	<0.001*
DTI	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	NA	NA	2429047	0.548	<0.001	<0.001*
DTI	Mean RD in tapetum R	0.07 ± 0.01	0.06 ± 0.01	NA	NA	2503302	0.623	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2660054	0.794	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	2746210	0.865	<0.001	<0.001*
rs-fMRI	Spos_1	14.77 ± 3.83	13.99 ± 3.49	10.78 ± 2.79	13.54 ± 3.26	688.8757	0.177	<0.001	<0.001*
rs-fMRI	Spos_2	27.86 ± 4.21	23.91 ± 3.88	24.18 ± 3.90	24.23 ± 3.72	454.3812	0.116	<0.001	<0.001*
rs-fMRI	Spos_3	18.15 ± 3.91	16.40 ± 3.81	12.65 ± 3.06	16.01 ± 3.46	922.4997	0.237	<0.001	<0.001*
rs-fMRI	Spos_4	26.71 ± 4.16	24.53 ± 3.93	20.73 ± 4.01	23.69 ± 3.72	812.0255	0.208	<0.001	<0.001*
rs-fMRI	Spos_5	30.50 ± 3.97	28.71 ± 3.51	28.20 ± 3.69	27.38 ± 3.48	275.4915	0.070	<0.001	<0.001*
rs-fMRI	Spos_6	16.82 ± 3.65	13.73 ± 3.65	12.88 ± 3.60	14.03 ± 3.50	471.1921	0.121	<0.001	<0.001*
rs-fMRI	Spos_7	22.83 ± 4.30	19.49 ± 3.60	22.66 ± 3.93	23.29 ± 3.64	592.8996	0.152	<0.001	<0.001*
rs-fMRI	Spos_8	20.80 ± 4.47	19.74 ± 4.52	16.08 ± 3.90	19.38 ± 4.03	562.3041	0.144	<0.001	<0.001*
rs-fMRI	Spos_9	21.28 ± 4.07	18.88 ± 3.80	18.19 ± 3.53	18.87 ± 3.29	282.8607	0.072	<0.001	<0.001*
rs-fMRI	Spos_10	25.62 ± 3.96	24.88 ± 3.68	24.48 ± 3.64	24.10 ± 3.58	67.73669	0.017	<0.001	<0.001*
rs-fMRI	Spos_11	32.42 ± 3.68	30.63 ± 3.46	31.42 ± 3.50	30.98 ± 3.39	118.9049	0.030	<0.001	<0.001*
rs-fMRI	Spos_12	28.65 ± 3.67	26.57 ± 3.29	27.64 ± 3.19	27.30 ± 3.28	169.661	0.043	<0.001	<0.001*
rs-fMRI	Spos_13	22.80 ± 3.86	20.31 ± 3.36	23.12 ± 3.51	24.10 ± 3.56	587.6567	0.151	<0.001	<0.001*
rs-fMRI	Spos_14	22.20 ± 4.06	20.55 ± 3.82	17.30 ± 3.39	19.60 ± 3.44	703.1548	0.180	<0.001	<0.001*
rs-fMRI	Spos_15	21.97 ± 4.00	18.27 ± 3.44	19.75 ± 3.58	20.47 ± 3.57	452.4931	0.116	<0.001	<0.001*
rs-fMRI	Spos_16	13.81 ± 4.15	13.78 ± 4.12	9.04 ± 3.30	13.17 ± 3.86	906.859	0.233	<0.001	<0.001*
rs-fMRI	Spos_17	15.35 ± 4.15	14.00 ± 3.48	13.30 ± 3.31	14.01 ± 3.32	123.805	0.031	<0.001	<0.001*
rs-fMRI	Spos_18	25.55 ± 4.09	22.73 ± 3.62	22.90 ± 3.77	23.29 ± 3.57	260.5902	0.066	<0.001	<0.001*
rs-fMRI	Spos_19	23.81 ± 3.64	22.20 ± 3.55	21.81 ± 3.58	22.20 ± 3.41	131.9326	0.033	<0.001	<0.001*
rs-fMRI	Spos_20	15.84 ± 3.62	13.21 ± 3.30	12.14 ± 3.25	14.22 ± 3.21	483.2402	0.124	<0.001	<0.001*
rs-fMRI	Spos_21	24.09 ± 3.97	20.98 ± 3.48	24.17 ± 3.56	24.63 ± 3.41	642.2369	0.165	<0.001	<0.001*
rs-fMRI	Spos_22	20.83 ± 4.08	17.91 ± 3.75	17.39 ± 3.81	18.42 ± 3.81	332.0213	0.085	<0.001	<0.001*
rs-fMRI	Spos_23	13.68 ± 3.72	11.67 ± 3.10	10.62 ± 2.79	11.69 ± 2.88	342.8586	0.088	<0.001	<0.001*
rs-fMRI	Spos_24	32.93 ± 4.11	32.20 ± 3.80	30.74 ± 3.88	30.37 ± 3.60	246.2868	0.063	<0.001	<0.001*
rs-fMRI	Spos_25	26.35 ± 4.11	23.24 ± 3.82	24.34 ± 3.75	25.57 ± 3.79	123.601	NA	<0.001	<0.001*
rs-fMRI	Spos_26	23.79 ± 3.54	22.61 ± 3.35	22.56 ± 3.32	22.95 ± 3.33	59.30017	0.014	<0.001	<0.001*
rs-fMRI	Spos_27	20.33 ± 4.36	17.83 ± 4.25	17.69 ± 3.85	20.89 ± 4.28	408.3153	0.104	<0.001	<0.001*
rs-fMRI	Spos_28	21.18 ± 3.77	18.47 ± 3.50	19.98 ± 3.56	20.22 ± 3.26	265.7858	0.068	<0.001	<0.001*
rs-fMRI	Spos_29	29.51 ± 3.74	27.47 ± 3.71	26.76 ± 3.68	26.01 ± 3.51	344.4398	0.088	<0.001	<0.001*
rs-fMRI	Spos_30	14.29 ± 3.88	12.66 ± 3.61	10.87 ± 2.96	13.33 ± 3.46	430.8961	0.110	<0.001	<0.001*

rs-fMRI	Spos_31	29.32 ± 4.18	25.92 ± 3.62	28.46 ± 3.98	28.60 ± 3.86	417.0145	0.107	<0.001	<0.001*
rs-fMRI	Spos_32	16.24 ± 3.93	13.69 ± 3.56	12.28 ± 3.13	14.43 ± 3.44	500.2906	0.128	<0.001	<0.001*
rs-fMRI	Spos_33	22.45 ± 3.79	20.54 ± 3.46	21.88 ± 3.75	21.95 ± 3.52	149.2241	0.038	<0.001	<0.001*
rs-fMRI	Spos_34	18.61 ± 3.60	18.57 ± 3.36	17.62 ± 3.15	18.43 ± 3.01	54.95136	0.013	<0.001	<0.001*
rs-fMRI	Spos_35	19.65 ± 4.04	16.91 ± 3.79	15.97 ± 3.40	17.75 ± 3.47	394.2585	0.101	<0.001	<0.001*
rs-fMRI	Spos_36	24.13 ± 3.91	24.29 ± 3.64	23.68 ± 3.55	23.74 ± 3.60	21.23803	0.005	<0.001	<0.001*
rs-fMRI	Spos_37	29.27 ± 4.29	25.50 ± 3.78	27.87 ± 3.94	28.38 ± 3.81	444.8414	0.114	<0.001	<0.001*
rs-fMRI	Spos_38	15.15 ± 3.76	11.85 ± 3.22	11.25 ± 3.04	12.10 ± 3.10	533.2611	0.137	<0.001	<0.001*
rs-fMRI	Spos_39	32.63 ± 3.93	31.94 ± 3.50	30.59 ± 3.79	31.35 ± 3.47	137.0509	0.035	<0.001	<0.001*
rs-fMRI	Spos_40	19.02 ± 3.92	17.34 ± 3.58	19.18 ± 3.87	20.85 ± 3.59	416.5253	0.106	<0.001	<0.001*
rs-fMRI	Spos_41	22.20 ± 4.43	20.04 ± 4.27	16.32 ± 3.26	19.07 ± 3.72	839.6135	0.215	<0.001	<0.001*
rs-fMRI	Spos_42	20.69 ± 3.84	19.10 ± 3.69	17.40 ± 3.42	19.04 ± 3.48	328.2219	0.084	<0.001	<0.001*
rs-fMRI	Spos_43	9.88 ± 3.05	9.20 ± 2.55	9.10 ± 2.57	9.88 ± 2.54	64.77375	0.016	<0.001	<0.001*
rs-fMRI	Spos_44	24.59 ± 4.00	21.31 ± 3.48	24.64 ± 3.69	25.03 ± 3.46	648.6035	0.166	<0.001	<0.001*
rs-fMRI	Spos_45	21.78 ± 3.95	18.87 ± 3.53	21.97 ± 3.86	23.37 ± 3.56	718.8138	0.184	<0.001	<0.001*
rs-fMRI	Spos_46	17.49 ± 4.38	17.13 ± 4.17	16.92 ± 4.19	16.93 ± 4.23	8.06196	0.001	0.045	0.045*
rs-fMRI	Spos_47	23.74 ± 4.52	20.11 ± 3.76	23.13 ± 4.33	23.88 ± 4.12	535.9515	0.137	<0.001	<0.001*
rs-fMRI	Spos_48	23.36 ± 3.89	22.18 ± 3.66	22.02 ± 3.53	21.94 ± 3.39	67.59027	0.017	<0.001	<0.001*
rs-fMRI	Spos_49	31.68 ± 4.39	30.90 ± 4.16	28.91 ± 4.13	28.38 ± 3.80	353.5399	0.090	<0.001	<0.001*
rs-fMRI	Spos_50	11.88 ± 3.33	11.11 ± 2.76	11.78 ± 2.99	12.10 ± 3.00	63.33114	0.016	<0.001	<0.001*
rs-fMRI	Spos_51	13.12 ± 3.50	11.81 ± 2.93	11.24 ± 2.86	11.87 ± 2.83	146.5769	0.037	<0.001	<0.001*
rs-fMRI	Spos_52	13.12 ± 3.46	12.32 ± 2.91	11.84 ± 2.85	12.55 ± 2.73	72.58232	0.018	<0.001	<0.001*
rs-fMRI	Spos_53	14.70 ± 4.20	12.54 ± 3.23	14.04 ± 3.80	14.38 ± 3.63	197.5477	0.050	<0.001	<0.001*
rs-fMRI	Spos_54	12.08 ± 3.27	11.49 ± 2.87	11.27 ± 2.89	12.01 ± 2.86	50.5655	0.012	<0.001	<0.001*
rs-fMRI	Spos_55	10.39 ± 2.20	8.88 ± 1.89	9.67 ± 2.07	10.08 ± 2.03	285.8523	0.073	<0.001	<0.001*
rs-fMRI	Sneg_1	20.09 ± 5.26	20.79 ± 5.44	13.70 ± 4.44	20.45 ± 5.12	1049.028	0.269	<0.001	<0.001*
rs-fMRI	Sneg_2	27.08 ± 3.95	28.54 ± 4.07	28.40 ± 4.21	30.46 ± 4.09	93.756	NA	<0.001	<0.001*
rs-fMRI	Sneg_3	19.19 ± 4.28	20.45 ± 4.20	15.77 ± 3.57	20.77 ± 4.12	805.6153	0.207	<0.001	<0.001*
rs-fMRI	Sneg_4	28.26 ± 5.67	30.85 ± 5.51	23.70 ± 5.70	30.75 ± 5.27	852.9181	0.219	<0.001	<0.001*
rs-fMRI	Sneg_5	27.04 ± 3.99	30.12 ± 4.48	29.37 ± 4.35	30.81 ± 4.45	319.7221	0.082	<0.001	<0.001*
rs-fMRI	Sneg_6	20.96 ± 6.72	20.22 ± 7.30	18.22 ± 7.23	21.82 ± 7.06	133.7279	0.034	<0.001	<0.001*
rs-fMRI	Sneg_7	22.11 ± 3.87	21.29 ± 3.52	23.77 ± 4.08	25.61 ± 4.19	589.3081	0.151	<0.001	<0.001*
rs-fMRI	Sneg_8	20.38 ± 6.29	21.16 ± 6.59	15.27 ± 4.96	21.32 ± 5.54	644.7498	0.165	<0.001	<0.001*
rs-fMRI	Sneg_9	19.70 ± 4.18	20.20 ± 4.34	18.95 ± 3.51	21.06 ± 3.96	132.2133	0.033	<0.001	<0.001*
rs-fMRI	Sneg_10	24.01 ± 4.69	26.33 ± 4.82	25.96 ± 5.11	26.45 ± 4.68	129.7055	0.033	<0.001	<0.001*

rs-fMRI	Sneg_11	25.31 ± 3.90	27.76 ± 4.06	27.70 ± 3.93	28.74 ± 3.84	109.498	NA	<0.001	<0.001*
rs-fMRI	Sneg_12	28.67 ± 4.85	30.26 ± 4.78	32.15 ± 4.35	33.17 ± 4.27	410.2224	0.105	<0.001	<0.001*
rs-fMRI	Sneg_13	22.09 ± 3.72	21.01 ± 3.64	22.73 ± 3.82	24.87 ± 3.91	461.291	0.118	<0.001	<0.001*
rs-fMRI	Sneg_14	23.93 ± 5.03	26.78 ± 5.15	19.97 ± 4.68	25.81 ± 4.91	897.6857	0.230	<0.001	<0.001*
rs-fMRI	Sneg_15	22.46 ± 4.22	22.08 ± 4.20	23.21 ± 4.13	25.68 ± 4.22	348.4136	0.089	<0.001	<0.001*
rs-fMRI	Sneg_16	14.96 ± 5.67	17.62 ± 6.51	9.69 ± 4.41	16.83 ± 6.10	1065.026	0.274	<0.001	<0.001*
rs-fMRI	Sneg_17	20.05 ± 4.07	18.01 ± 3.35	18.41 ± 3.64	19.49 ± 3.55	171.6946	0.043	<0.001	<0.001*
rs-fMRI	Sneg_18	24.84 ± 4.68	26.85 ± 4.67	26.75 ± 4.97	28.89 ± 4.66	268.8041	0.068	<0.001	<0.001*
rs-fMRI	Sneg_19	23.48 ± 5.19	24.77 ± 5.14	23.80 ± 5.06	25.78 ± 4.98	102.1593	0.026	<0.001	<0.001*
rs-fMRI	Sneg_20	19.24 ± 5.48	19.84 ± 5.91	16.57 ± 5.42	21.70 ± 5.79	374.7176	0.096	<0.001	<0.001*
rs-fMRI	Sneg_21	21.22 ± 4.17	19.62 ± 3.72	22.23 ± 4.40	23.67 ± 4.40	457.1689	0.117	<0.001	<0.001*
rs-fMRI	Sneg_22	17.84 ± 4.39	18.02 ± 4.22	17.50 ± 4.24	19.61 ± 4.35	117.3395	0.029	<0.001	<0.001*
rs-fMRI	Sneg_23	17.96 ± 4.06	16.77 ± 3.76	15.59 ± 3.16	17.26 ± 3.50	190.6604	0.048	<0.001	<0.001*
rs-fMRI	Sneg_24	26.62 ± 4.04	29.24 ± 4.13	28.25 ± 4.14	29.36 ± 3.99	227.2403	0.058	<0.001	<0.001*
rs-fMRI	Sneg_25	21.04 ± 4.08	21.66 ± 4.17	22.11 ± 4.26	24.52 ± 4.12	316.917	0.081	<0.001	<0.001*
rs-fMRI	Sneg_26	23.90 ± 4.08	25.64 ± 4.45	25.99 ± 4.63	27.17 ± 4.20	219.5224	0.056	<0.001	<0.001*
rs-fMRI	Sneg_27	22.29 ± 3.79	20.96 ± 3.74	21.07 ± 3.83	23.83 ± 3.95	301.1348	0.077	<0.001	<0.001*
rs-fMRI	Sneg_28	20.13 ± 5.12	20.21 ± 4.88	23.45 ± 5.32	24.31 ± 5.40	445.0636	0.114	<0.001	<0.001*
rs-fMRI	Sneg_29	21.42 ± 4.52	24.59 ± 4.84	23.15 ± 4.45	24.73 ± 4.61	262.9769	0.067	<0.001	<0.001*
rs-fMRI	Sneg_30	17.16 ± 5.19	17.27 ± 5.78	14.96 ± 4.61	19.06 ± 5.29	290.644	0.074	<0.001	<0.001*
rs-fMRI	Sneg_31	23.37 ± 4.08	23.82 ± 4.11	26.10 ± 4.35	27.40 ± 4.17	485.49	0.124	<0.001	<0.001*
rs-fMRI	Sneg_32	16.97 ± 5.38	17.35 ± 6.11	14.13 ± 4.75	19.06 ± 5.63	385.6668	0.099	<0.001	<0.001*
rs-fMRI	Sneg_33	20.97 ± 4.20	21.41 ± 4.17	23.23 ± 4.50	24.53 ± 4.51	342.1867	0.087	<0.001	<0.001*
rs-fMRI	Sneg_34	24.73 ± 4.63	25.26 ± 4.78	24.60 ± 4.53	25.80 ± 4.65	34.10004	0.008	<0.001	<0.001*
rs-fMRI	Sneg_35	18.46 ± 3.68	18.08 ± 3.74	17.67 ± 3.54	19.98 ± 3.65	194.6375	0.049	<0.001	<0.001*
rs-fMRI	Sneg_36	24.48 ± 4.17	24.89 ± 4.16	24.84 ± 4.21	26.49 ± 4.01	112.7024	0.028	<0.001	<0.001*
rs-fMRI	Sneg_37	23.68 ± 4.21	24.10 ± 4.15	25.01 ± 4.41	27.80 ± 4.19	165.926	NA	<0.001	<0.001*
rs-fMRI	Sneg_38	13.08 ± 3.25	13.05 ± 3.19	12.27 ± 2.99	14.17 ± 3.21	170.631	0.043	<0.001	<0.001*
rs-fMRI	Sneg_39	26.23 ± 4.75	29.24 ± 4.74	26.85 ± 4.95	29.48 ± 4.62	294.755	0.075	<0.001	<0.001*
rs-fMRI	Sneg_40	22.44 ± 3.69	21.21 ± 3.58	22.69 ± 3.84	23.82 ± 3.94	220.0507	0.056	<0.001	<0.001*
rs-fMRI	Sneg_41	19.52 ± 5.56	21.13 ± 6.03	16.49 ± 3.77	20.93 ± 4.77	523.9142	0.134	<0.001	<0.001*
rs-fMRI	Sneg_42	21.00 ± 4.05	22.69 ± 4.10	20.10 ± 3.80	22.96 ± 3.87	324.3731	0.083	<0.001	<0.001*
rs-fMRI	Sneg_43	18.51 ± 4.29	15.88 ± 3.45	16.22 ± 3.61	16.50 ± 3.48	221.0914	0.056	<0.001	<0.001*
rs-fMRI	Sneg_44	21.62 ± 3.80	20.96 ± 3.61	22.95 ± 3.63	24.78 ± 3.65	526.577	0.135	<0.001	<0.001*
rs-fMRI	Sneg_45	17.86 ± 3.61	17.18 ± 3.14	18.78 ± 3.74	20.53 ± 3.68	435.2748	0.111	<0.001	<0.001*

rs-fMRI	Sneg_46	18.22 ± 3.46	18.63 ± 3.57	18.36 ± 3.33	19.59 ± 3.65	67.20925	0.017	<0.001	<0.001*
rs-fMRI	Sneg_47	16.82 ± 3.98	15.51 ± 3.57	17.35 ± 4.03	18.86 ± 3.87	372.0074	0.095	<0.001	<0.001*
rs-fMRI	Sneg_48	19.62 ± 4.06	21.26 ± 4.38	20.22 ± 4.20	21.97 ± 4.10	149.0587	0.038	<0.001	<0.001*
rs-fMRI	Sneg_49	18.08 ± 3.75	20.76 ± 3.93	18.95 ± 3.63	20.67 ± 3.79	301.6913	0.077	<0.001	<0.001*
rs-fMRI	Sneg_50	17.23 ± 3.94	15.44 ± 3.07	15.93 ± 3.23	16.46 ± 3.21	124.1701	0.031	<0.001	<0.001*
rs-fMRI	Sneg_51	18.31 ± 4.01	17.24 ± 3.56	16.75 ± 3.44	17.83 ± 3.37	89.9156	0.022	<0.001	<0.001*
rs-fMRI	Sneg_52	17.58 ± 3.83	16.35 ± 3.28	15.67 ± 3.23	16.92 ± 3.27	140.7738	0.035	<0.001	<0.001*
rs-fMRI	Sneg_53	14.55 ± 4.68	13.13 ± 3.58	14.05 ± 3.83	15.43 ± 4.42	173.0727	0.044	<0.001	<0.001*
rs-fMRI	Sneg_54	16.65 ± 4.12	14.81 ± 3.43	14.71 ± 3.50	15.46 ± 3.39	131.7861	0.033	<0.001	<0.001*
rs-fMRI	Sneg_55	10.70 ± 2.24	10.64 ± 1.99	10.81 ± 1.97	11.30 ± 1.96	63.07367	0.015	<0.001	<0.001*
t-fMRI	Median z-statistic (amygdala) for faces-shapes contrast	0.74 ± 0.72	1.73 ± 0.78	NA	NA	616239.5	-1.305	<0.001	<0.001*
t-fMRI	Median z-statistic for faces activation	1.77 ± 1.07	3.57 ± 0.95	NA	NA	315885	-1.806	<0.001	<0.001*
t-fMRI	Median z-statistic for shapes activation	1.81 ± 1.18	3.20 ± 1.14	NA	NA	698117	-1.200	<0.001	<0.001*
t-fMRI	Median z-statistic for faces-shapes contrast	1.67 ± 1.14	3.43 ± 1.16	NA	NA	476701	-1.531	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic (amygdala) for faces-shapes contrast	2.42 ± 0.81	3.55 ± 0.96	NA	NA	645696	-1.256	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces activation	4.80 ± 1.46	7.36 ± 1.22	NA	NA	246315.5	-1.941	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for shapes activation	4.54 ± 1.54	6.49 ± 1.45	NA	NA	619629.5	-1.312	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces-shapes contrast	4.82 ± 1.56	7.46 ± 1.48	NA	NA	358615.5	-1.749	<0.001	<0.001*
PGSs	ADHD Demontis2022	0.30 ± 0.54	0.28 ± 0.56	NA	NA	1.035548	0.033	0.300	0.373
PGSs	ALCDEP Walters2018	-1.15 ± 0.19	-1.14 ± 0.20	NA	NA	1841056	-0.047	0.174	0.238
PGSs	AN Watson2019	-4.37 ± 0.58	-4.34 ± 0.62	NA	NA	1846575	-0.047	0.230	0.300
PGSs	ASD Grove2019	-0.35 ± 0.36	-0.36 ± 0.35	NA	NA	1.026241	0.033	0.305	0.373
PGSs	BD PGC4 2025	-1.47 ± 0.56	-1.45 ± 0.57	NA	NA	1859274	-0.044	0.402	0.464
PGSs	BMI Locke2015	0.33 ± 0.21	0.31 ± 0.21	NA	NA	2.507572	0.080	0.012	0.022*
PGSs	bNGF Konieczny2025	0.00 ± 0.03	-0.02 ± 0.03	NA	NA	22.00377	0.706	<0.001	<0.001*
PGSs	CAD Nikpay2015	0.92 ± 0.40	0.92 ± 0.38	NA	NA	0.240499	0.008	0.810	0.853
PGSs	CCL11 Konieczny2025	-0.76 ± 0.26	-0.79 ± 0.26	NA	NA	1987827	0.093	0.005	0.009*
PGSs	CCL2 Konieczny2025	0.24 ± 0.53	0.30 ± 0.58	NA	NA	1813222	-0.097	0.031	0.049*
PGSs	CCL3 Konieczny2025	-0.44 ± 0.32	-0.47 ± 0.32	NA	NA	1966109	0.078	0.027	0.043*
PGSs	CCL4 Konieczny2025	0.54 ± 0.41	0.56 ± 0.40	NA	NA	1837115	-0.052	0.141	0.197
PGSs	CCL7 Konieczny2025	-0.91 ± 0.38	-0.98 ± 0.39	NA	NA	2077699	0.171	<0.001	<0.001*
PGSs	CRP Said2022	0.30 ± 0.39	0.26 ± 0.39	NA	NA	2.818096	0.090	0.005	0.009*
PGSs	CSF1 Konieczny2025	0.68 ± 0.64	0.73 ± 0.65	NA	NA	1810204	-0.081	0.025	0.042*

PGSs	CSF3 Konieczny2025	0.49 ± 0.30	0.46 ± 0.29	NA	NA	1997300	0.106	0.002	0.004*
PGSs	CTACK Konieczny2025	-0.01 ± 0.04	-0.06 ± 0.05	NA	NA	2989602	1.129	<0.001	<0.001*
PGSs	CUD Johnson2020	-1.13 ± 0.32	-1.13 ± 0.32	NA	NA	1901709	0.006	0.708	0.758
PGSs	CXCL1 Konieczny2025	-3.37 ± 0.73	-3.39 ± 0.73	NA	NA	1921378	0.028	0.349	0.417
PGSs	CXCL10 Konieczny2025	-0.07 ± 0.10	-0.13 ± 0.10	NA	NA	19.24723	0.617	<0.001	<0.001*
PGSs	CXCL12 Konieczny2025	0.19 ± 0.13	0.15 ± 0.13	NA	NA	9.208558	0.295	<0.001	<0.001*
PGSs	CXCL9 Konieczny2025	0.01 ± 0.08	-0.05 ± 0.08	NA	NA	21.98064	0.705	<0.001	<0.001*
PGSs	FGFb Konieczny2025	0.54 ± 0.37	0.53 ± 0.37	NA	NA	1905941	0.022	0.620	0.689
PGSs	GAD FinnGen2024	0.15 ± 0.29	0.13 ± 0.29	NA	NA	1.506429	0.048	0.132	0.189
PGSs	HbA1c Willems2023	0.11 ± 0.07	0.12 ± 0.07	NA	NA	-1.61708	-0.052	0.106	0.155
PGSs	HDL Graham2021	1.88 ± 0.43	1.91 ± 0.43	NA	NA	1806290	-0.064	0.019	0.032*
PGSs	HGF Konieczny2025	0.38 ± 0.12	0.33 ± 0.12	NA	NA	12.64069	0.405	<0.001	<0.001*
PGSs	IFNg Konieczny2025	0.16 ± 0.08	0.05 ± 0.08	NA	NA	3188215	1.424	<0.001	<0.001*
PGSs	IL10 Konieczny2025	0.07 ± 0.04	0.02 ± 0.04	NA	NA	35.84691	1.150	<0.001	<0.001*
PGSs	IL13 Konieczny2025	0.05 ± 0.08	-0.07 ± 0.07	NA	NA	3341895	1.689	<0.001	<0.001*
PGSs	IL16 Konieczny2025	0.31 ± 0.46	0.27 ± 0.47	NA	NA	1990104	0.099	0.004	0.007*
PGSs	IL17 Konieczny2025	0.09 ± 0.04	0.03 ± 0.04	NA	NA	3284988	1.578	<0.001	<0.001*
PGSs	IL18 Konieczny2025	1.27 ± 1.11	1.29 ± 1.10	NA	NA	1873469	-0.012	0.665	0.726
PGSs	IL1b Konieczny2025	-0.77 ± 0.17	-0.78 ± 0.17	NA	NA	1925865	0.048	0.287	0.366
PGSs	IL1RA Konieczny2025	-0.29 ± 0.17	-0.33 ± 0.17	NA	NA	7.47257	0.240	<0.001	<0.001*
PGSs	IL2 Konieczny2025	0.19 ± 0.07	0.16 ± 0.07	NA	NA	16.4781	0.529	<0.001	<0.001*
PGSs	IL2RA Konieczny2025	0.09 ± 0.07	0.07 ± 0.07	NA	NA	2192060	0.291	<0.001	<0.001*
PGSs	IL4 Konieczny2025	0.09 ± 0.04	0.03 ± 0.03	NA	NA	3348532	1.688	<0.001	<0.001*
PGSs	IL5 Konieczny2025	0.11 ± 0.04	0.06 ± 0.04	NA	NA	3280655	1.565	<0.001	<0.001*
PGSs	IL6 Konieczny2025	0.10 ± 0.06	0.06 ± 0.05	NA	NA	2557939	0.660	<0.001	<0.001*
PGSs	IL7 Konieczny2025	0.00 ± 0.03	-0.05 ± 0.03	NA	NA	3370500	1.732	<0.001	<0.001*
PGSs	IL8 Konieczny2025	0.19 ± 0.08	0.11 ± 0.08	NA	NA	31.88017	1.022	<0.001	<0.001*
PGSs	IL9 Konieczny2025	0.16 ± 0.07	0.09 ± 0.08	NA	NA	2791588	0.918	<0.001	<0.001*
PGSs	LDL Graham2021	0.33 ± 0.41	0.30 ± 0.40	NA	NA	1961953	0.070	0.036	0.055
PGSs	MDD PGC4 2025	-0.91 ± 0.36	-0.91 ± 0.37	NA	NA	1888900	0.009	0.993	0.993
PGSs	MIF Konieczny2025	0.04 ± 0.04	0.03 ± 0.04	NA	NA	2155868	0.254	<0.001	<0.001*
PGSs	NEUROT DeMoor2015	-0.15 ± 0.05	-0.15 ± 0.05	NA	NA	1.307755	0.042	0.191	0.255
PGSs	OCD PGC3 2018	-0.04 ± 0.31	-0.04 ± 0.32	NA	NA	0.121396	0.004	0.903	0.919
PGSs	PDGFBB Konieczny2025	0.23 ± 0.16	0.17 ± 0.15	NA	NA	2335862	0.423	<0.001	<0.001*
PGSs	PTSD Nievergelt2024	-0.44 ± 0.29	-0.46 ± 0.29	NA	NA	1952230	0.060	0.069	0.103

PGSs	RANTES Konieczny2025	0.22 ± 0.17	0.15 ± 0.17	NA	NA	2300565	0.383	<0.001	<0.001*
PGSs	SCF Konieczny2025	0.85 ± 0.23	0.85 ± 0.23	NA	NA	0.743788	0.024	0.457	0.517
PGSs	SCGFb Konieczny2025	-0.01 ± 0.25	-0.06 ± 0.24	NA	NA	2111017	0.217	<0.001	<0.001*
PGSs	SCZ Trubetskoy2022	-5.16 ± 1.04	-5.13 ± 1.10	NA	NA	1856225	-0.027	0.355	0.417
PGSs	T2D Verma2024	-12.51 ± 0.93	-12.57 ± 1.00	NA	NA	1975078	0.060	0.013	0.024*
PGSs	TNFa Konieczny2025	0.10 ± 0.03	0.04 ± 0.03	NA	NA	3389717	1.757	<0.001	<0.001*
PGSs	TNFb Konieczny2025	0.09 ± 0.04	0.02 ± 0.04	NA	NA	3440303	1.849	<0.001	<0.001*
PGSs	TRAIL Konieczny2025	-0.27 ± 0.35	-0.26 ± 0.35	NA	NA	1882836	-0.008	0.869	0.899
PGSs	TRIG Graham2021	-1.44 ± 0.38	-1.50 ± 0.38	NA	NA	2063136	0.167	<0.001	<0.001*
PGSs	VEGF Konieczny2025	-0.58 ± 0.29	-0.62 ± 0.29	NA	NA	2034996	0.133	<0.001	<0.001*
Multimodal	Area of caudalanteriorcingulate L	1063.90 ± 168.72	1075.67 ± 220.66	NA	NA	1839610	-0.060	0.195	0.264
Multimodal	Area of caudalanteriorcingulate R	762.24 ± 158.37	774.66 ± 167.57	NA	NA	1803181	-0.076	0.019	0.031*
Multimodal	Area of caudalmiddlefrontal L	2338.14 ± 341.38	2342.70 ± 361.58	NA	NA	1888036	-0.013	0.927	0.949
Multimodal	Area of caudalmiddlefrontal R	2172.70 ± 337.06	2180.08 ± 349.11	NA	NA	1874366	-0.022	0.764	0.812
Multimodal	Area of cuneus L	2092.37 ± 279.35	2071.84 ± 282.45	NA	NA	1964563	0.073	0.023	0.036*
Multimodal	Area of cuneus R	2000.65 ± 254.40	1992.32 ± 262.59	NA	NA	1933712	0.032	0.162	0.224
Multimodal	Area of entorhinal L	419.10 ± 73.96	420.82 ± 77.20	NA	NA	1867170	-0.023	0.613	0.689
Multimodal	Area of entorhinal R	371.64 ± 68.30	375.76 ± 69.59	NA	NA	1828685	-0.060	0.108	0.155
Multimodal	Area of fusiform L	2811.41 ± 333.63	2825.48 ± 350.25	NA	NA	1848836	-0.041	0.303	0.381
Multimodal	Area of fusiform R	2741.16 ± 345.18	2764.35 ± 354.32	NA	NA	1808454	-0.066	0.029	0.045*
Multimodal	Area of inferiorparietal L	4321.30 ± 597.53	4354.01 ± 602.18	NA	NA	1815792	-0.055	0.048	0.072
Multimodal	Area of inferiorparietal R	5047.08 ± 683.23	5085.65 ± 707.54	NA	NA	1823095	-0.055	0.077	0.113
Multimodal	Area of inferiortemporal L	3354.69 ± 436.10	3378.89 ± 440.03	NA	NA	1815945	-0.055	0.049	0.073
Multimodal	Area of inferiortemporal R	3530.75 ± 456.37	3563.33 ± 460.86	NA	NA	1787411	-0.071	0.005	0.009*
Multimodal	Area of insula L	1954.81 ± 190.86	1963.67 ± 197.01	NA	NA	1834306	-0.046	0.148	0.208
Multimodal	Area of insula R	2042.73 ± 201.24	2053.58 ± 202.58	NA	NA	1816794	-0.054	0.051	0.077
Multimodal	Area of isthmuscingulate L	1001.92 ± 155.70	1005.65 ± 163.33	NA	NA	1877451	-0.023	0.832	0.871
Multimodal	Area of isthmuscingulate R	894.75 ± 134.29	893.02 ± 144.02	NA	NA	1922650	0.012	0.280	0.358
Multimodal	Area of lateraloccipital L	4987.14 ± 581.10	4999.78 ± 607.90	NA	NA	1872086	-0.021	0.715	0.768
Multimodal	Area of lateraloccipital R	5071.12 ± 624.08	5082.99 ± 651.27	NA	NA	1880972	-0.019	0.912	0.940
Multimodal	Area of lateralorbitofrontal L	2947.47 ± 297.25	2966.33 ± 307.87	NA	NA	1826153	-0.062	0.093	0.135
Multimodal	Area of lateralorbitofrontal R	2953.91 ± 313.29	2964.97 ± 324.35	NA	NA	1848509	-0.035	0.298	0.380
Multimodal	Area of lingual L	3153.91 ± 386.73	3130.30 ± 391.75	NA	NA	1952210	0.061	0.054	0.080
Multimodal	Area of lingual R	3219.80 ± 403.70	3202.16 ± 421.28	NA	NA	1941941	0.043	0.102	0.147
Multimodal	Area of medialorbitofrontal L	1579.85 ± 169.99	1589.14 ± 171.77	NA	NA	1827059	-0.054	0.098	0.142

Multimodal	Area of medialorbitofrontal R	1496.82 ± 159.95	1510.41 ± 166.04	NA	NA	1789218	-0.083	0.006	0.011*
Multimodal	Area of middletemporal L	4112.18 ± 512.75	4138.91 ± 525.08	NA	NA	1828760	-0.052	0.108	0.155
Multimodal	Area of middletemporal R	4126.33 ± 474.60	4143.27 ± 482.07	NA	NA	1842381	-0.035	0.224	0.298
Multimodal	Area of paracentral L	1589.75 ± 190.60	1593.73 ± 193.93	NA	NA	1868032	-0.021	0.630	0.701
Multimodal	Area of paracentral R	1568.29 ± 196.15	1577.68 ± 203.76	NA	NA	1842855	-0.047	0.229	0.303
Multimodal	Area of parahippocampal L	697.57 ± 80.55	695.51 ± 80.06	NA	NA	1902927	0.026	0.605	0.685
Multimodal	Area of parahippocampal R	674.48 ± 78.67	676.62 ± 77.12	NA	NA	1850519	-0.027	0.326	0.403
Multimodal	Area of parsopercularis L	1432.51 ± 202.65	1441.33 ± 218.34	NA	NA	1857210	-0.042	0.429	0.516
Multimodal	Area of parsopercularis R	1518.59 ± 213.60	1526.53 ± 224.51	NA	NA	1859757	-0.036	0.473	0.559
Multimodal	Area of parsorbitalis L	672.86 ± 80.53	677.96 ± 80.48	NA	NA	1808505	-0.063	0.029	0.045*
Multimodal	Area of parsorbitalis R	688.81 ± 93.81	696.03 ± 98.10	NA	NA	1808388	-0.075	0.029	0.045*
Multimodal	Area of parstriangularis L	1539.33 ± 236.11	1548.05 ± 241.13	NA	NA	1848748	-0.037	0.302	0.381
Multimodal	Area of parstriangularis R	1447.03 ± 226.10	1455.95 ± 228.27	NA	NA	1835175	-0.039	0.155	0.216
Multimodal	Area of pericalcarine L	1408.79 ± 242.12	1378.82 ± 242.18	NA	NA	2019063	0.124	<0.001	<0.001*
Multimodal	Area of pericalcarine R	1548.17 ± 255.34	1524.97 ± 262.82	NA	NA	1985772	0.090	0.004	0.007*
Multimodal	Area of postcentral L	4575.88 ± 482.90	4576.80 ± 498.25	NA	NA	1882994	-0.002	0.958	0.969
Multimodal	Area of postcentral R	4333.25 ± 494.74	4332.97 ± 511.71	NA	NA	1881471	0.001	0.923	0.948
Multimodal	Area of posteriorcingulate L	1248.75 ± 171.49	1254.27 ± 186.86	NA	NA	1861565	-0.031	0.505	0.589
Multimodal	Area of posteriorcingulate R	1206.17 ± 172.42	1208.46 ± 188.19	NA	NA	1880975	-0.013	0.912	0.940
Multimodal	Area of precentral L	4631.31 ± 462.43	4633.59 ± 484.40	NA	NA	1872258	-0.005	0.719	0.770
Multimodal	Area of precentral R	4494.29 ± 466.08	4505.75 ± 483.49	NA	NA	1860835	-0.024	0.492	0.578
Multimodal	Area of precuneus L	3670.61 ± 458.98	3678.90 ± 463.43	NA	NA	1867703	-0.018	0.624	0.697
Multimodal	Area of precuneus R	4019.45 ± 501.82	4004.75 ± 502.12	NA	NA	1910585	0.029	0.462	0.548
Multimodal	Area of rostralanteriorcingulate L	1160.94 ± 193.37	1169.43 ± 197.91	NA	NA	1843984	-0.043	0.242	0.318
Multimodal	Area of rostralanteriorcingulate R	796.91 ± 152.91	809.46 ± 156.49	NA	NA	1791368	-0.081	0.007	0.013*
Multimodal	Area of rostralmiddlefrontal L	3897.00 ± 544.21	3925.40 ± 568.99	NA	NA	1834891	-0.051	0.153	0.213
Multimodal	Area of rostralmiddlefrontal R	4038.06 ± 574.37	4065.87 ± 600.87	NA	NA	1838982	-0.047	0.189	0.257
Multimodal	Area of superiorfrontal L	7660.65 ± 846.42	7690.44 ± 891.25	NA	NA	1853997	-0.034	0.377	0.460
Multimodal	Area of superiorfrontal R	8749.97 ± 1000.44	8782.89 ± 1032.11	NA	NA	1858250	-0.032	0.446	0.533
Multimodal	Area of superiorparietal L	4254.47 ± 540.02	4265.91 ± 554.87	NA	NA	1862419	-0.021	0.521	0.602
Multimodal	Area of superiorparietal R	4343.21 ± 530.63	4347.29 ± 554.48	NA	NA	1877113	-0.008	0.825	0.868
Multimodal	Area of superiortemporal L	5014.23 ± 525.05	5035.98 ± 549.09	NA	NA	1855892	-0.041	0.407	0.493
Multimodal	Area of superiortemporal R	4694.64 ± 447.69	4708.28 ± 468.29	NA	NA	1866430	-0.030	0.598	0.679
Multimodal	Area of supramarginal L	3580.18 ± 556.88	3579.86 ± 572.97	NA	NA	1884686	0.001	0.996	0.996
Multimodal	Area of supramarginal R	3392.62 ± 471.33	3375.67 ± 483.52	NA	NA	1916684	0.036	0.362	0.443

Multimodal	Area of transversetemporal L	448.24 ± 69.76	445.88 ± 70.53	NA	NA	1927981	0.034	0.217	0.291
Multimodal	Area of transversetemporal R	327.26 ± 45.56	327.15 ± 47.37	NA	NA	1901095	0.002	0.642	0.710
Multimodal	Volume of caudalanteriorcingulate L	3154.08 ± 564.68	3129.40 ± 600.84	NA	NA	1953887	0.042	0.048	0.072
Multimodal	Volume of caudalanteriorcingulate R	2269.52 ± 573.44	2279.81 ± 558.23	NA	NA	1854584	-0.018	0.386	0.469
Multimodal	Volume of caudalmiddlefrontal L	7327.84 ± 1111.28	7096.07 ± 1142.63	NA	NA	2117818	0.206	<0.001	<0.001*
Multimodal	Volume of caudalmiddlefrontal R	6764.67 ± 1102.46	6572.58 ± 1111.79	NA	NA	2091248	0.174	<0.001	<0.001*
Multimodal	Volume of cuneus L	4491.12 ± 698.87	4282.94 ± 691.68	NA	NA	2215836	0.299	<0.001	<0.001*
Multimodal	Volume of cuneus R	4034.47 ± 640.17	3866.18 ± 620.11	NA	NA	2181830	0.267	<0.001	<0.001*
Multimodal	Volume of entorhinal L	1812.35 ± 339.74	1745.40 ± 339.94	NA	NA	2100611	0.197	<0.001	<0.001*
Multimodal	Volume of entorhinal R	1730.53 ± 328.10	1663.55 ± 319.45	NA	NA	2104372	0.207	<0.001	<0.001*
Multimodal	Volume of fusiform L	9308.03 ± 1199.64	9072.49 ± 1208.44	NA	NA	2098722	0.196	<0.001	<0.001*
Multimodal	Volume of fusiform R	9057.91 ± 1246.87	8854.00 ± 1244.03	NA	NA	2065595	0.164	<0.001	<0.001*
Multimodal	Volume of inferiorparietal L	12884.95 ± 1783.41	12584.75 ± 1775.25	NA	NA	2063582	0.169	<0.001	<0.001*
Multimodal	Volume of inferiorparietal R	15347.59 ± 2066.25	14979.79 ± 2101.07	NA	NA	2067012	0.177	<0.001	<0.001*
Multimodal	Volume of inferior temporal L	12678.11 ± 1663.03	12469.06 ± 1665.47	NA	NA	2020414	0.126	<0.001	<0.001*
Multimodal	Volume of inferior temporal R	12896.68 ± 1711.98	12605.45 ± 1672.63	NA	NA	2061816	0.172	<0.001	<0.001*
Multimodal	Volume of insula L	6377.31 ± 659.73	6301.84 ± 662.45	NA	NA	2010118	0.114	<0.001	<0.001*
Multimodal	Volume of insula R	6608.34 ± 682.04	6517.63 ± 695.00	NA	NA	2034057	0.132	<0.001	<0.001*
Multimodal	Volume of isthmuscingulate L	2750.46 ± 437.89	2696.18 ± 438.29	NA	NA	2019460	0.124	<0.001	<0.001*
Multimodal	Volume of isthmuscingulate R	2616.80 ± 405.55	2552.57 ± 417.69	NA	NA	2067051	0.156	<0.001	<0.001*
Multimodal	Volume of lateraloccipital L	12818.82 ± 1643.91	12373.67 ± 1695.57	NA	NA	2184786	0.267	<0.001	<0.001*
Multimodal	Volume of lateraloccipital R	13126.54 ± 1785.95	12671.58 ± 1792.74	NA	NA	2168605	0.254	<0.001	<0.001*
Multimodal	Volume of lateralorbitofrontal L	9335.03 ± 964.81	9150.04 ± 982.43	NA	NA	2107048	0.190	<0.001	<0.001*
Multimodal	Volume of lateralorbitofrontal R	9314.61 ± 949.79	9122.15 ± 957.10	NA	NA	2115843	0.202	<0.001	<0.001*
Multimodal	Volume of lingual L	6820.22 ± 1093.29	6517.58 ± 1097.98	NA	NA	2188249	0.276	<0.001	<0.001*
Multimodal	Volume of lingual R	6788.73 ± 1082.35	6520.34 ± 1091.75	NA	NA	2152274	0.247	<0.001	<0.001*
Multimodal	Volume of medialorbitofrontal L	5104.04 ± 580.51	5011.19 ± 584.43	NA	NA	2055676	0.159	<0.001	<0.001*
Multimodal	Volume of medialorbitofrontal R	4946.15 ± 553.50	4882.74 ± 551.55	NA	NA	2011313	0.115	<0.001	<0.001*
Multimodal	Volume of middletemporal L	14369.27 ± 1878.16	14044.48 ± 1898.40	NA	NA	2071869	0.172	<0.001	<0.001*
Multimodal	Volume of middletemporal R	14589.35 ± 1786.62	14230.47 ± 1772.26	NA	NA	2101555	0.202	<0.001	<0.001*
Multimodal	Volume of paracentral L	4757.87 ± 575.87	4573.24 ± 582.34	NA	NA	2229571	0.319	<0.001	<0.001*
Multimodal	Volume of paracentral R	4592.96 ± 607.65	4433.79 ± 604.81	NA	NA	2166281	0.262	<0.001	<0.001*
Multimodal	Volume of parahippocampal L	2242.37 ± 322.96	2145.24 ± 307.92	NA	NA	2213144	0.307	<0.001	<0.001*
Multimodal	Volume of parahippocampal R	2105.24 ± 275.07	2040.73 ± 264.27	NA	NA	2139628	0.239	<0.001	<0.001*
Multimodal	Volume of parsopercularis L	4656.96 ± 694.17	4551.82 ± 721.29	NA	NA	2071263	0.149	<0.001	<0.001*

Multimodal	Volume of parsopercularis R	4774.81 ± 709.78	4672.94 ± 721.19	NA	NA	2050076	0.142	<0.001	<0.001*
Multimodal	Volume of parsorbitalis L	2317.43 ± 312.19	2265.28 ± 308.60	NA	NA	2056513	0.168	<0.001	<0.001*
Multimodal	Volume of parsorbitalis R	2383.33 ± 342.83	2330.57 ± 350.19	NA	NA	2057512	0.152	<0.001	<0.001*
Multimodal	Volume of parstriangularis L	4632.37 ± 750.46	4527.73 ± 757.16	NA	NA	2048757	0.139	<0.001	<0.001*
Multimodal	Volume of parstriangularis R	4276.89 ± 716.20	4187.03 ± 701.64	NA	NA	2014703	0.127	<0.001	<0.001*
Multimodal	Volume of pericalcarine L	2168.09 ± 438.09	2057.20 ± 417.33	NA	NA	2155735	0.259	<0.001	<0.001*
Multimodal	Volume of pericalcarine R	2335.21 ± 452.66	2238.42 ± 444.94	NA	NA	2114632	0.216	<0.001	<0.001*
Multimodal	Volume of postcentral L	11989.97 ± 1446.54	11529.51 ± 1451.47	NA	NA	2228950	0.318	<0.001	<0.001*
Multimodal	Volume of postcentral R	11166.57 ± 1440.13	10764.73 ± 1439.34	NA	NA	2183172	0.279	<0.001	<0.001*
Multimodal	Volume of posteriorcingulate L	3641.01 ± 516.58	3582.54 ± 533.58	NA	NA	2005602	0.111	<0.001	<0.001*
Multimodal	Volume of posteriorcingulate R	3692.47 ± 536.15	3625.64 ± 532.29	NA	NA	2023240	0.125	<0.001	<0.001*
Multimodal	Volume of precentral L	14439.58 ± 1614.85	13876.76 ± 1610.92	NA	NA	2258285	0.349	<0.001	<0.001*
Multimodal	Volume of precentral R	13875.59 ± 1575.80	13364.51 ± 1600.52	NA	NA	2233476	0.322	<0.001	<0.001*
Multimodal	Volume of precuneus L	10657.10 ± 1285.63	10316.95 ± 1264.56	NA	NA	2175077	0.267	<0.001	<0.001*
Multimodal	Volume of precuneus R	11404.78 ± 1368.93	10980.10 ± 1331.69	NA	NA	2209276	0.314	<0.001	<0.001*
Multimodal	Volume of rostralanteriorcingulate L	3788.62 ± 628.71	3729.37 ± 619.49	NA	NA	1994143	0.095	0.002	0.003*
Multimodal	Volume of rostralanteriorcingulate R	2692.17 ± 531.18	2680.01 ± 525.69	NA	NA	1907682	0.023	0.514	0.595
Multimodal	Volume of rostralmiddlefrontal L	11877.04 ± 1653.16	11587.78 ± 1713.20	NA	NA	2080288	0.172	<0.001	<0.001*
Multimodal	Volume of rostralmiddlefrontal R	11961.97 ± 1727.45	11729.66 ± 1782.24	NA	NA	2036409	0.132	<0.001	<0.001*
Multimodal	Volume of superiorfrontal L	26124.70 ± 2852.40	25306.19 ± 2884.89	NA	NA	2196910	0.285	<0.001	<0.001*
Multimodal	Volume of superiorfrontal R	29001.81 ± 3310.41	28181.99 ± 3306.98	NA	NA	2162200	0.248	<0.001	<0.001*
Multimodal	Volume of superiorparietal L	11781.11 ± 1518.65	11423.84 ± 1553.11	NA	NA	2129184	0.233	<0.001	<0.001*
Multimodal	Volume of superiorparietal R	11924.66 ± 1514.54	11509.81 ± 1561.02	NA	NA	2172802	0.270	<0.001	<0.001*
Multimodal	Volume of superiortemporal L	17663.15 ± 1921.75	17147.65 ± 1959.72	NA	NA	2183533	0.266	<0.001	<0.001*
Multimodal	Volume of superiortemporal R	16783.02 ± 1683.78	16275.16 ± 1708.57	NA	NA	2215665	0.299	<0.001	<0.001*
Multimodal	Volume of supramarginal L	11108.87 ± 1693.38	10748.10 ± 1684.09	NA	NA	2113864	0.214	<0.001	<0.001*
Multimodal	Volume of supramarginal R	10515.36 ± 1455.49	10126.36 ± 1459.55	NA	NA	2169572	0.267	<0.001	<0.001*
Multimodal	Volume of transversetemporal L	1268.78 ± 228.37	1224.79 ± 227.45	NA	NA	2097901	0.193	<0.001	<0.001*
Multimodal	Volume of transversetemporal R	1010.59 ± 170.51	972.70 ± 172.77	NA	NA	2134616	0.221	<0.001	<0.001*
Multimodal	Mean thickness of caudalanteriorcingulate L	2.77 ± 0.27	2.74 ± 0.27	NA	NA	2024580	0.121	<0.001	<0.001*
Multimodal	Mean thickness of caudalanteriorcingulate R	2.54 ± 0.32	2.54 ± 0.33	NA	NA	1923616	0.026	0.267	0.345
Multimodal	Mean thickness of caudalmiddlefrontal L	2.92 ± 0.13	2.84 ± 0.14	NA	NA	2478834	0.580	<0.001	<0.001*
Multimodal	Mean thickness of caudalmiddlefrontal R	2.88 ± 0.13	2.80 ± 0.13	NA	NA	17.66751	0.567	<0.001	<0.001*
Multimodal	Mean thickness of cuneus L	2.08 ± 0.14	2.02 ± 0.14	NA	NA	2380828	0.465	<0.001	<0.001*
Multimodal	Mean thickness of cuneus R	1.98 ± 0.14	1.92 ± 0.13	NA	NA	2351402	0.442	<0.001	<0.001*

Multimodal	Mean thickness of entorhinal L	3.32 ± 0.27	3.21 ± 0.29	NA	NA	2299318	0.388	<0.001	<0.001*
Multimodal	Mean thickness of entorhinal R	3.40 ± 0.30	3.29 ± 0.32	NA	NA	2282684	0.379	<0.001	<0.001*
Multimodal	Mean thickness of fusiform L	2.93 ± 0.12	2.86 ± 0.13	NA	NA	2419958	0.513	<0.001	<0.001*
Multimodal	Mean thickness of fusiform R	2.92 ± 0.13	2.86 ± 0.14	NA	NA	2395021	0.487	<0.001	<0.001*
Multimodal	Mean thickness of inferiorparietal L	2.75 ± 0.11	2.68 ± 0.11	NA	NA	2525928	0.620	<0.001	<0.001*
Multimodal	Mean thickness of inferiorparietal R	2.78 ± 0.11	2.71 ± 0.12	NA	NA	2489554	0.592	<0.001	<0.001*
Multimodal	Mean thickness of inferior temporal L	3.08 ± 0.13	3.03 ± 0.14	NA	NA	2296107	0.391	<0.001	<0.001*
Multimodal	Mean thickness of inferior temporal R	3.06 ± 0.13	2.99 ± 0.13	NA	NA	14.93854	0.480	<0.001	<0.001*
Multimodal	Mean thickness of insula L	3.23 ± 0.15	3.18 ± 0.17	NA	NA	2252432	0.356	<0.001	<0.001*
Multimodal	Mean thickness of insula R	3.23 ± 0.15	3.16 ± 0.16	NA	NA	2328743	0.425	<0.001	<0.001*
Multimodal	Mean thickness of isthmuscingulate L	2.51 ± 0.18	2.46 ± 0.17	NA	NA	2185978	0.298	<0.001	<0.001*
Multimodal	Mean thickness of isthmuscingulate R	2.57 ± 0.19	2.52 ± 0.19	NA	NA	2150639	0.255	<0.001	<0.001*
Multimodal	Mean thickness of lateraloccipital L	2.36 ± 0.12	2.29 ± 0.12	NA	NA	17.95373	0.576	<0.001	<0.001*
Multimodal	Mean thickness of lateraloccipital R	2.39 ± 0.13	2.32 ± 0.13	NA	NA	2415621	0.523	<0.001	<0.001*
Multimodal	Mean thickness of lateralorbitofrontal L	2.87 ± 0.13	2.81 ± 0.14	NA	NA	13.10252	0.421	<0.001	<0.001*
Multimodal	Mean thickness of lateralorbitofrontal R	2.85 ± 0.13	2.80 ± 0.14	NA	NA	11.20892	0.360	<0.001	<0.001*
Multimodal	Mean thickness of lingual L	2.07 ± 0.14	2.00 ± 0.15	NA	NA	2354440	0.452	<0.001	<0.001*
Multimodal	Mean thickness of lingual R	2.04 ± 0.14	1.98 ± 0.15	NA	NA	12.21613	0.392	<0.001	<0.001*
Multimodal	Mean thickness of medialorbitofrontal L	2.68 ± 0.16	2.64 ± 0.17	NA	NA	2188999	0.281	<0.001	<0.001*
Multimodal	Mean thickness of medialorbitofrontal R	2.71 ± 0.18	2.67 ± 0.18	NA	NA	2136347	0.219	<0.001	<0.001*
Multimodal	Mean thickness of middletemporal L	2.95 ± 0.14	2.88 ± 0.15	NA	NA	2378825	0.470	<0.001	<0.001*
Multimodal	Mean thickness of middletemporal R	3.03 ± 0.13	2.96 ± 0.14	NA	NA	2396497	0.491	<0.001	<0.001*
Multimodal	Mean thickness of paracentral L	2.77 ± 0.17	2.67 ± 0.18	NA	NA	2469699	0.560	<0.001	<0.001*
Multimodal	Mean thickness of paracentral R	2.75 ± 0.17	2.66 ± 0.18	NA	NA	2435352	0.533	<0.001	<0.001*
Multimodal	Mean thickness of parahippocampal L	2.84 ± 0.29	2.75 ± 0.29	NA	NA	2241351	0.318	<0.001	<0.001*
Multimodal	Mean thickness of parahippocampal R	2.76 ± 0.24	2.69 ± 0.25	NA	NA	2191239	0.277	<0.001	<0.001*
Multimodal	Mean thickness of parsopercularis L	2.92 ± 0.13	2.85 ± 0.14	NA	NA	2399589	0.501	<0.001	<0.001*
Multimodal	Mean thickness of parsopercularis R	2.87 ± 0.13	2.80 ± 0.13	NA	NA	2364954	0.474	<0.001	<0.001*
Multimodal	Mean thickness of parsorbitalis L	2.93 ± 0.16	2.86 ± 0.16	NA	NA	13.85942	0.445	<0.001	<0.001*
Multimodal	Mean thickness of parsorbitalis R	2.94 ± 0.17	2.86 ± 0.17	NA	NA	2357562	0.443	<0.001	<0.001*
Multimodal	Mean thickness of parstriangularis L	2.75 ± 0.12	2.69 ± 0.13	NA	NA	2408085	0.508	<0.001	<0.001*
Multimodal	Mean thickness of parstriangularis R	2.72 ± 0.12	2.66 ± 0.13	NA	NA	2365697	0.468	<0.001	<0.001*
Multimodal	Mean thickness of pericalcarine L	1.77 ± 0.14	1.71 ± 0.14	NA	NA	2307588	0.402	<0.001	<0.001*
Multimodal	Mean thickness of pericalcarine R	1.73 ± 0.14	1.68 ± 0.14	NA	NA	2253402	0.347	<0.001	<0.001*
Multimodal	Mean thickness of postcentral L	2.40 ± 0.12	2.33 ± 0.13	NA	NA	2490485	0.593	<0.001	<0.001*

Multimodal	Mean thickness of postcentral R	2.35 ± 0.14	2.28 ± 0.14	NA	NA	2438694	0.506	<0.001	<0.001*
Multimodal	Mean thickness of posteriorcingulate L	2.72 ± 0.16	2.67 ± 0.17	NA	NA	2194397	0.314	<0.001	<0.001*
Multimodal	Mean thickness of posteriorcingulate R	2.73 ± 0.16	2.69 ± 0.18	NA	NA	2162782	0.257	<0.001	<0.001*
Multimodal	Mean thickness of precentral L	2.90 ± 0.15	2.80 ± 0.16	NA	NA	2527173	0.612	<0.001	<0.001*
Multimodal	Mean thickness of precentral R	2.85 ± 0.16	2.75 ± 0.17	NA	NA	2514948	0.587	<0.001	<0.001*
Multimodal	Mean thickness of precuneus L	2.68 ± 0.12	2.61 ± 0.13	NA	NA	2483796	0.581	<0.001	<0.001*
Multimodal	Mean thickness of precuneus R	2.68 ± 0.12	2.60 ± 0.12	NA	NA	19.13649	0.614	<0.001	<0.001*
Multimodal	Mean thickness of rostralanteriorcingulate L	2.93 ± 0.17	2.88 ± 0.18	NA	NA	2170122	0.264	<0.001	<0.001*
Multimodal	Mean thickness of rostralanteriorcingulate R	2.97 ± 0.19	2.93 ± 0.20	NA	NA	2096684	0.188	<0.001	<0.001*
Multimodal	Mean thickness of rostralmiddlefrontal L	2.73 ± 0.11	2.66 ± 0.12	NA	NA	2492823	0.592	<0.001	<0.001*
Multimodal	Mean thickness of rostralmiddlefrontal R	2.67 ± 0.10	2.62 ± 0.11	NA	NA	2418042	0.520	<0.001	<0.001*
Multimodal	Mean thickness of superiorfrontal L	3.01 ± 0.12	2.93 ± 0.13	NA	NA	2575883	0.686	<0.001	<0.001*
Multimodal	Mean thickness of superiorfrontal R	2.97 ± 0.11	2.89 ± 0.12	NA	NA	2559317	0.671	<0.001	<0.001*
Multimodal	Mean thickness of superiorparietal L	2.53 ± 0.11	2.46 ± 0.12	NA	NA	2481039	0.571	<0.001	<0.001*
Multimodal	Mean thickness of superiorparietal R	2.51 ± 0.12	2.44 ± 0.13	NA	NA	2475395	0.574	<0.001	<0.001*
Multimodal	Mean thickness of superiortemporal L	3.04 ± 0.15	2.96 ± 0.16	NA	NA	2472624	0.549	<0.001	<0.001*
Multimodal	Mean thickness of superiortemporal R	3.11 ± 0.14	3.03 ± 0.15	NA	NA	2476209	0.574	<0.001	<0.001*
Multimodal	Mean thickness of supramarginal L	2.88 ± 0.12	2.80 ± 0.13	NA	NA	2529887	0.630	<0.001	<0.001*
Multimodal	Mean thickness of supramarginal R	2.88 ± 0.12	2.80 ± 0.13	NA	NA	18.9857	0.610	<0.001	<0.001*
Multimodal	Mean thickness of transversetemporal L	2.59 ± 0.25	2.52 ± 0.24	NA	NA	9.449946	0.303	<0.001	<0.001*
Multimodal	Mean thickness of transversetemporal R	2.65 ± 0.26	2.56 ± 0.26	NA	NA	2242320	0.331	<0.001	<0.001*
Multimodal	Volume of accumbens L	536.07 ± 109.10	508.88 ± 117.82	NA	NA	2145930	0.240	<0.001	<0.001*
Multimodal	Volume of accumbens R	428.46 ± 101.67	407.24 ± 103.09	NA	NA	2086770	0.207	<0.001	<0.001*
Multimodal	Volume of amygdala L	1261.41 ± 247.67	1231.10 ± 242.27	NA	NA	2018607	0.124	<0.001	<0.001*
Multimodal	Volume of amygdala R	1225.95 ± 273.07	1192.93 ± 266.02	NA	NA	1999122	0.122	0.001	0.002*
Multimodal	Volume of caudate L	3383.90 ± 402.66	3383.95 ± 401.64	NA	NA	1882884	0.000	0.955	0.969
Multimodal	Volume of caudate R	3553.44 ± 423.03	3551.39 ± 421.06	NA	NA	1886484	0.005	0.963	0.969
Multimodal	Volume of hippocampus L	3888.60 ± 447.85	3808.15 ± 470.76	NA	NA	2066780	0.175	<0.001	<0.001*
Multimodal	Volume of hippocampus R	3999.58 ± 437.86	3919.87 ± 476.75	NA	NA	2053256	0.174	<0.001	<0.001*
Multimodal	Volume of pallidum L	1764.54 ± 227.97	1736.43 ± 234.19	NA	NA	2034208	0.122	<0.001	<0.001*
Multimodal	Volume of pallidum R	1819.89 ± 226.93	1787.77 ± 231.82	NA	NA	2039278	0.140	<0.001	<0.001*
Multimodal	Volume of putamen L	4868.70 ± 556.32	4825.86 ± 560.85	NA	NA	1975030	0.077	0.010	0.016*
Multimodal	Volume of putamen R	4904.09 ± 553.82	4863.42 ± 564.48	NA	NA	1971989	0.073	0.013	0.021*
Multimodal	Volume of thalamus L	7928.83 ± 733.41	7756.67 ± 750.40	NA	NA	2142611	0.232	<0.001	<0.001*
Multimodal	Volume of thalamus R	7733.49 ± 716.14	7553.64 ± 736.19	NA	NA	2163359	0.248	<0.001	<0.001*

Multimodal	Mean FA in anterior corona radiata L	0.48 ± 0.02	0.45 ± 0.02	NA	NA	3075728	1.283	<0.001	<0.001*
Multimodal	Mean FA in anterior corona radiata R	0.48 ± 0.02	0.45 ± 0.02	NA	NA	3026599	1.220	<0.001	<0.001*
Multimodal	Mean FA in anterior limb of internal capsule L	0.60 ± 0.02	0.58 ± 0.02	NA	NA	2910943	1.044	<0.001	<0.001*
Multimodal	Mean FA in anterior limb of internal capsule R	0.61 ± 0.02	0.59 ± 0.02	NA	NA	2851753	0.978	<0.001	<0.001*
Multimodal	Mean FA in body of corpus callosum	0.73 ± 0.02	0.70 ± 0.02	NA	NA	3117763	1.298	<0.001	<0.001*
Multimodal	Mean FA in cerebral peduncle L	0.73 ± 0.02	0.71 ± 0.02	NA	NA	2783463	0.886	<0.001	<0.001*
Multimodal	Mean FA in cerebral peduncle R	0.72 ± 0.02	0.70 ± 0.02	NA	NA	2837594	0.961	<0.001	<0.001*
Multimodal	Mean FA in cingulum cingulate gyrus L	0.64 ± 0.03	0.61 ± 0.03	NA	NA	2843972	0.963	<0.001	<0.001*
Multimodal	Mean FA in cingulum cingulate gyrus R	0.60 ± 0.03	0.57 ± 0.03	NA	NA	2828613	0.956	<0.001	<0.001*
Multimodal	Mean FA in cingulum hippocampus L	0.48 ± 0.03	0.45 ± 0.03	NA	NA	2551838	0.646	<0.001	<0.001*
Multimodal	Mean FA in cingulum hippocampus R	0.47 ± 0.03	0.45 ± 0.03	NA	NA	2517518	0.613	<0.001	<0.001*
Multimodal	Mean FA in corticospinal tract L	0.55 ± 0.03	0.53 ± 0.03	NA	NA	2495459	0.580	<0.001	<0.001*
Multimodal	Mean FA in corticospinal tract R	0.53 ± 0.03	0.51 ± 0.04	NA	NA	2415589	0.511	<0.001	<0.001*
Multimodal	Mean FA in external capsule L	0.48 ± 0.02	0.46 ± 0.02	NA	NA	2823504	0.955	<0.001	<0.001*
Multimodal	Mean FA in external capsule R	0.47 ± 0.02	0.45 ± 0.02	NA	NA	2862793	0.999	<0.001	<0.001*
Multimodal	Mean FA in fornix cres+stria terminalis L	0.55 ± 0.03	0.53 ± 0.03	NA	NA	2629508	0.724	<0.001	<0.001*
Multimodal	Mean FA in fornix cres+stria terminalis R	0.55 ± 0.03	0.52 ± 0.03	NA	NA	2655493	0.755	<0.001	<0.001*
Multimodal	Mean FA in fornix	0.48 ± 0.07	0.46 ± 0.08	NA	NA	2276996	0.372	<0.001	<0.001*
Multimodal	Mean FA in genu of corpus callosum	0.75 ± 0.02	0.71 ± 0.03	NA	NA	3113562	1.287	<0.001	<0.001*
Multimodal	Mean FA in inferior cerebellar peduncle L	0.56 ± 0.03	0.54 ± 0.03	NA	NA	2648979	0.707	<0.001	<0.001*
Multimodal	Mean FA in inferior cerebellar peduncle R	0.56 ± 0.02	0.55 ± 0.03	NA	NA	2667867	0.735	<0.001	<0.001*
Multimodal	Mean FA in medial lemniscus L	0.60 ± 0.02	0.58 ± 0.03	NA	NA	2583124	0.679	<0.001	<0.001*
Multimodal	Mean FA in medial lemniscus R	0.60 ± 0.02	0.59 ± 0.03	NA	NA	2586806	0.678	<0.001	<0.001*
Multimodal	Mean FA in middle cerebellar peduncle	0.55 ± 0.02	0.54 ± 0.02	NA	NA	2657035	0.760	<0.001	<0.001*
Multimodal	Mean FA in pontine crossing tract	0.41 ± 0.03	0.40 ± 0.03	NA	NA	2284228	0.374	<0.001	<0.001*
Multimodal	Mean FA in posterior corona radiata L	0.50 ± 0.02	0.47 ± 0.02	NA	NA	3130479	1.313	<0.001	<0.001*
Multimodal	Mean FA in posterior corona radiata R	0.51 ± 0.02	0.48 ± 0.02	NA	NA	3075527	1.242	<0.001	<0.001*
Multimodal	Mean FA in posterior limb of internal capsule L	0.70 ± 0.02	0.68 ± 0.02	NA	NA	2632233	0.731	<0.001	<0.001*
Multimodal	Mean FA in posterior limb of internal capsule R	0.69 ± 0.02	0.67 ± 0.02	NA	NA	2618790	0.727	<0.001	<0.001*
Multimodal	Mean FA in posterior thalamic radiation L	0.63 ± 0.02	0.60 ± 0.03	NA	NA	3009436	1.161	<0.001	<0.001*
Multimodal	Mean FA in posterior thalamic radiation R	0.62 ± 0.02	0.59 ± 0.03	NA	NA	3040870	1.220	<0.001	<0.001*
Multimodal	Mean FA in retrolenticular part of internal capsule L	0.63 ± 0.02	0.61 ± 0.02	NA	NA	2785916	0.900	<0.001	<0.001*
Multimodal	Mean FA in retrolenticular part of internal capsule R	0.61 ± 0.02	0.58 ± 0.03	NA	NA	2757833	0.882	<0.001	<0.001*
Multimodal	Mean FA in sagittal stratum L	0.58 ± 0.03	0.56 ± 0.03	NA	NA	2866912	0.994	<0.001	<0.001*

Multimodal	Mean FA in sagittal stratum R	0.58 ± 0.02	0.55 ± 0.03	NA	NA	3001067	1.160	<0.001	<0.001*
Multimodal	Mean FA in splenium of corpus callosum	0.80 ± 0.02	0.78 ± 0.02	NA	NA	2917774	1.013	<0.001	<0.001*
Multimodal	Mean FA in superior cerebellar peduncle L	0.72 ± 0.02	0.70 ± 0.02	NA	NA	2668330	0.742	<0.001	<0.001*
Multimodal	Mean FA in superior cerebellar peduncle R	0.70 ± 0.02	0.69 ± 0.02	NA	NA	2651326	0.730	<0.001	<0.001*
Multimodal	Mean FA in superior corona radiata L	0.51 ± 0.02	0.48 ± 0.02	NA	NA	2997197	1.162	<0.001	<0.001*
Multimodal	Mean FA in superior corona radiata R	0.50 ± 0.02	0.48 ± 0.02	NA	NA	2918195	1.063	<0.001	<0.001*
Multimodal	Mean FA in superior fronto-occipital fasciculus L	0.49 ± 0.03	0.46 ± 0.04	NA	NA	2695857	0.810	<0.001	<0.001*
Multimodal	Mean FA in superior fronto-occipital fasciculus R	0.48 ± 0.03	0.46 ± 0.04	NA	NA	2585920	0.688	<0.001	<0.001*
Multimodal	Mean FA in superior longitudinal fasciculus L	0.54 ± 0.02	0.52 ± 0.02	NA	NA	3037531	1.214	<0.001	<0.001*
Multimodal	Mean FA in superior longitudinal fasciculus R	0.54 ± 0.02	0.51 ± 0.02	NA	NA	3062280	1.240	<0.001	<0.001*
Multimodal	Mean FA in tapetum L	0.60 ± 0.06	0.57 ± 0.06	NA	NA	2399982	0.487	<0.001	<0.001*
Multimodal	Mean FA in tapetum R	0.58 ± 0.06	0.55 ± 0.06	NA	NA	2470213	0.573	<0.001	<0.001*
Multimodal	Mean FA in uncinate fasciculus L	0.52 ± 0.03	0.50 ± 0.04	NA	NA	2533800	0.628	<0.001	<0.001*
Multimodal	Mean FA in uncinate fasciculus R	0.54 ± 0.03	0.52 ± 0.03	NA	NA	2539870	0.639	<0.001	<0.001*
Multimodal	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1131007	-0.742	<0.001	<0.001*
Multimodal	Mean AD in anterior corona radiata R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1178035	-0.690	<0.001	<0.001*
Multimodal	Mean AD in anterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	NA	NA	1615946	-0.266	<0.001	<0.001*
Multimodal	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	NA	NA	1645892	-0.234	<0.001	<0.001*
Multimodal	Mean AD in body of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	NA	NA	1458744	-0.390	<0.001	<0.001*
Multimodal	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	1902845	0.020	0.607	0.686
Multimodal	Mean AD in cerebral peduncle R	0.14 ± 0.01	0.15 ± 0.01	NA	NA	1790653	-0.078	0.007	0.012*
Multimodal	Mean AD in cingulum cingulate gyrus L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	1711675	-0.143	<0.001	<0.001*
Multimodal	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	NA	NA	1722038	-0.146	<0.001	<0.001*
Multimodal	Mean AD in cingulum hippocampus L	0.12 ± 0.01	0.12 ± 0.01	NA	NA	1565473	-0.296	<0.001	<0.001*
Multimodal	Mean AD in cingulum hippocampus R	0.12 ± 0.01	0.12 ± 0.01	NA	NA	-9.30353	-0.299	<0.001	<0.001*
Multimodal	Mean AD in corticospinal tract L	0.13 ± 0.01	0.13 ± 0.01	NA	NA	1733621	-0.146	<0.001	<0.001*
Multimodal	Mean AD in corticospinal tract R	0.13 ± 0.01	0.13 ± 0.01	NA	NA	1744506	-0.135	<0.001	<0.001*
Multimodal	Mean AD in external capsule L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1368863	-0.499	<0.001	<0.001*
Multimodal	Mean AD in external capsule R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1326134	-0.534	<0.001	<0.001*
Multimodal	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.14 ± 0.01	NA	NA	1599822	-0.268	<0.001	<0.001*
Multimodal	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	NA	NA	1521846	-0.345	<0.001	<0.001*
Multimodal	Mean AD in fornix	0.22 ± 0.02	0.23 ± 0.02	NA	NA	1652283	-0.242	<0.001	<0.001*
Multimodal	Mean AD in genu of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	NA	NA	1364636	-0.491	<0.001	<0.001*
Multimodal	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1731886	-0.141	<0.001	<0.001*

Multimodal	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1746414	-0.125	<0.001	<0.001*
Multimodal	Mean AD in medial lemniscus L	0.13 ± 0.01	0.14 ± 0.01	NA	NA	1776701	-0.094	0.002	0.003*
Multimodal	Mean AD in medial lemniscus R	0.13 ± 0.01	0.14 ± 0.01	NA	NA	1821286	-0.069	0.069	0.102
Multimodal	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	NA	NA	-8.41207	-0.270	<0.001	<0.001*
Multimodal	Mean AD in pontine crossing tract	0.11 ± 0.01	0.12 ± 0.01	NA	NA	1656273	-0.202	<0.001	<0.001*
Multimodal	Mean AD in posterior corona radiata L	0.12 ± 0.00	0.13 ± 0.01	NA	NA	1084266	-0.780	<0.001	<0.001*
Multimodal	Mean AD in posterior corona radiata R	0.13 ± 0.00	0.13 ± 0.01	NA	NA	1138808	-0.729	<0.001	<0.001*
Multimodal	Mean AD in posterior limb of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	NA	NA	1728222	-0.159	<0.001	<0.001*
Multimodal	Mean AD in posterior limb of internal capsule R	0.14 ± 0.00	0.14 ± 0.00	NA	NA	1680079	-0.201	<0.001	<0.001*
Multimodal	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	NA	NA	1367382	-0.485	<0.001	<0.001*
Multimodal	Mean AD in posterior thalamic radiation R	0.15 ± 0.00	0.15 ± 0.01	NA	NA	1404708	-0.457	<0.001	<0.001*
Multimodal	Mean AD in retrolenticular part of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	NA	NA	1456325	-0.400	<0.001	<0.001*
Multimodal	Mean AD in retrolenticular part of internal capsule R	0.13 ± 0.00	0.14 ± 0.00	NA	NA	1357861	-0.501	<0.001	<0.001*
Multimodal	Mean AD in sagittal stratum L	0.13 ± 0.00	0.14 ± 0.01	NA	NA	1293494	-0.568	<0.001	<0.001*
Multimodal	Mean AD in sagittal stratum R	0.14 ± 0.00	0.14 ± 0.01	NA	NA	1296324	-0.574	<0.001	<0.001*
Multimodal	Mean AD in splenium of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	NA	NA	1471124	-0.392	<0.001	<0.001*
Multimodal	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	NA	NA	1677352	-0.181	<0.001	<0.001*
Multimodal	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	NA	NA	1636907	-0.223	<0.001	<0.001*
Multimodal	Mean AD in superior corona radiata L	0.11 ± 0.00	0.12 ± 0.00	NA	NA	1303018	-0.576	<0.001	<0.001*
Multimodal	Mean AD in superior corona radiata R	0.11 ± 0.00	0.12 ± 0.00	NA	NA	1330451	-0.559	<0.001	<0.001*
Multimodal	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.01	0.12 ± 0.01	NA	NA	1434935	-0.442	<0.001	<0.001*
Multimodal	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.12 ± 0.01	NA	NA	1519977	-0.363	<0.001	<0.001*
Multimodal	Mean AD in superior longitudinal fasciculus L	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1242578	-0.627	<0.001	<0.001*
Multimodal	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	NA	NA	1248890	-0.616	<0.001	<0.001*
Multimodal	Mean AD in tapetum L	0.16 ± 0.01	0.16 ± 0.02	NA	NA	1529821	-0.348	<0.001	<0.001*
Multimodal	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	NA	NA	1521765	-0.355	<0.001	<0.001*
Multimodal	Mean AD in uncinate fasciculus L	0.12 ± 0.01	0.12 ± 0.01	NA	NA	-5.20739	-0.167	<0.001	<0.001*
Multimodal	Mean AD in uncinate fasciculus R	0.12 ± 0.01	0.12 ± 0.01	NA	NA	1731521	-0.146	<0.001	<0.001*
Multimodal	Mean RD in anterior corona radiata L	0.05 ± 0.00	0.06 ± 0.00	NA	NA	483669.5	-1.539	<0.001	<0.001*
Multimodal	Mean RD in anterior corona radiata R	0.05 ± 0.00	0.06 ± 0.00	NA	NA	507563.5	-1.518	<0.001	<0.001*
Multimodal	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	805846.5	-1.067	<0.001	<0.001*
Multimodal	Mean RD in anterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	853273.5	-0.991	<0.001	<0.001*

Multimodal	Mean RD in body of corpus callosum	0.04 ± 0.00	0.04 ± 0.00	NA	NA	579163	-1.381	<0.001	<0.001*
Multimodal	Mean RD in cerebral peduncle L	0.03 ± 0.00	0.04 ± 0.00	NA	NA	987493.5	-0.873	<0.001	<0.001*
Multimodal	Mean RD in cerebral peduncle R	0.03 ± 0.00	0.04 ± 0.00	NA	NA	910625.5	-0.969	<0.001	<0.001*
Multimodal	Mean RD in cingulum cingulate gyrus L	0.04 ± 0.00	0.05 ± 0.00	NA	NA	700056.5	-1.242	<0.001	<0.001*
Multimodal	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	713870.5	-1.240	<0.001	<0.001*
Multimodal	Mean RD in cingulum hippocampus L	0.05 ± 0.00	0.06 ± 0.00	NA	NA	944218	-0.914	<0.001	<0.001*
Multimodal	Mean RD in cingulum hippocampus R	0.05 ± 0.00	0.06 ± 0.00	NA	NA	961123.5	-0.917	<0.001	<0.001*
Multimodal	Mean RD in corticospinal tract L	0.05 ± 0.01	0.05 ± 0.01	NA	NA	1369205	-0.473	<0.001	<0.001*
Multimodal	Mean RD in corticospinal tract R	0.05 ± 0.01	0.06 ± 0.01	NA	NA	1450132	-0.391	<0.001	<0.001*
Multimodal	Mean RD in external capsule L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	807598.5	-1.102	<0.001	<0.001*
Multimodal	Mean RD in external capsule R	0.05 ± 0.00	0.06 ± 0.00	NA	NA	777956.5	-1.129	<0.001	<0.001*
Multimodal	Mean RD in fornix cres+stria terminalis L	0.05 ± 0.00	0.06 ± 0.01	NA	NA	1067426	-0.733	<0.001	<0.001*
Multimodal	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.00	0.06 ± 0.01	NA	NA	1031810	-0.793	<0.001	<0.001*
Multimodal	Mean RD in fornix	0.10 ± 0.03	0.11 ± 0.03	NA	NA	1557802	-0.302	<0.001	<0.001*
Multimodal	Mean RD in genu of corpus callosum	0.03 ± 0.00	0.04 ± 0.00	NA	NA	620494	-1.312	<0.001	<0.001*
Multimodal	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	947685	-0.858	<0.001	<0.001*
Multimodal	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	934937.5	-0.916	<0.001	<0.001*
Multimodal	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	1266116	-0.540	<0.001	<0.001*
Multimodal	Mean RD in medial lemniscus R	0.04 ± 0.00	0.05 ± 0.00	NA	NA	1278591	-0.533	<0.001	<0.001*
Multimodal	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	NA	NA	1061745	-0.795	<0.001	<0.001*
Multimodal	Mean RD in pontine crossing tract	0.06 ± 0.01	0.06 ± 0.01	NA	NA	1554167	-0.324	<0.001	<0.001*
Multimodal	Mean RD in posterior corona radiata L	0.05 ± 0.00	0.06 ± 0.00	NA	NA	490671.5	-1.387	<0.001	<0.001*
Multimodal	Mean RD in posterior corona radiata R	0.05 ± 0.00	0.06 ± 0.00	NA	NA	544223.5	-1.352	<0.001	<0.001*
Multimodal	Mean RD in posterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	979594	-0.905	<0.001	<0.001*
Multimodal	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	983782.5	-0.903	<0.001	<0.001*
Multimodal	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	654986	-1.216	<0.001	<0.001*
Multimodal	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	605344	-1.341	<0.001	<0.001*
Multimodal	Mean RD in retrolenticular part of internal capsule L	0.04 ± 0.00	0.05 ± 0.00	NA	NA	775755	-1.096	<0.001	<0.001*
Multimodal	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	779746	-1.101	<0.001	<0.001*
Multimodal	Mean RD in sagittal stratum L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	676880	-1.281	<0.001	<0.001*
Multimodal	Mean RD in sagittal stratum R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	590146	-1.370	<0.001	<0.001*
Multimodal	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.03 ± 0.00	NA	NA	701547	-1.172	<0.001	<0.001*
Multimodal	Mean RD in superior cerebellar peduncle L	0.04 ± 0.00	0.04 ± 0.00	NA	NA	1085194	-0.725	<0.001	<0.001*
Multimodal	Mean RD in superior cerebellar peduncle R	0.04 ± 0.00	0.04 ± 0.00	NA	NA	1092588	-0.753	<0.001	<0.001*

Multimodal	Mean RD in superior corona radiata L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	488791	-1.527	<0.001	<0.001*
Multimodal	Mean RD in superior corona radiata R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	552226	-1.430	<0.001	<0.001*
Multimodal	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.00	0.05 ± 0.01	NA	NA	877548	-0.800	<0.001	<0.001*
Multimodal	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.00	0.05 ± 0.01	NA	NA	927477.5	-0.834	<0.001	<0.001*
Multimodal	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	516010	-1.475	<0.001	<0.001*
Multimodal	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	520133.5	-1.470	<0.001	<0.001*
Multimodal	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	NA	NA	1338407	-0.514	<0.001	<0.001*
Multimodal	Mean RD in tapetum R	0.06 ± 0.01	0.07 ± 0.01	NA	NA	1275733	-0.574	<0.001	<0.001*
Multimodal	Mean RD in uncinate fasciculus L	0.05 ± 0.00	0.05 ± 0.00	NA	NA	1095767	-0.763	<0.001	<0.001*
Multimodal	Mean RD in uncinate fasciculus R	0.05 ± 0.00	0.05 ± 0.00	NA	NA	1042801	-0.803	<0.001	<0.001*
Multimodal	Median z-statistic (amygdala) for faces-shapes contrast	1.40 ± 0.92	1.29 ± 0.88	NA	NA	1993281	0.117	0.002	0.003*
Multimodal	Median z-statistic for faces activation	2.92 ± 1.30	2.81 ± 1.36	NA	NA	1966368	0.083	0.020	0.032*
Multimodal	Median z-statistic for shapes activation	2.69 ± 1.33	2.63 ± 1.36	NA	NA	1924408	0.048	0.258	0.336
Multimodal	Median z-statistic for faces-shapes contrast	2.80 ± 1.41	2.68 ± 1.46	NA	NA	1966161	0.084	0.020	0.032*
Multimodal	90th percentile of z-statistic (amygdala) for faces-shapes contrast	3.16 ± 1.09	3.05 ± 1.03	NA	NA	1989123	0.107	0.003	0.005*
Multimodal	90th percentile of z-statistic for faces activation	6.41 ± 1.77	6.30 ± 1.86	NA	NA	1946214	0.060	0.079	0.115
Multimodal	90th percentile of z-statistic for shapes activation	5.75 ± 1.75	5.71 ± 1.79	NA	NA	1907729	0.024	0.513	0.595
Multimodal	90th percentile of z-statistic for faces-shapes contrast	6.51 ± 1.92	6.36 ± 2.05	NA	NA	1964257	0.076	0.023	0.037*
Multimodal	Spos_1	13.14 ± 3.66	13.27 ± 3.67	NA	NA	1840708	-0.034	0.207	0.278
Multimodal	Spos_2	25.26 ± 4.24	24.36 ± 4.10	NA	NA	2106251	0.214	<0.001	<0.001*
Multimodal	Spos_3	15.76 ± 4.13	15.59 ± 3.99	NA	NA	1924555	0.041	0.256	0.335
Multimodal	Spos_4	23.86 ± 4.48	23.69 ± 4.45	NA	NA	1.236504	0.040	0.216	0.290
Multimodal	Spos_5	28.71 ± 3.82	28.57 ± 3.75	NA	NA	1919509	0.038	0.321	0.399
Multimodal	Spos_6	14.33 ± 3.81	14.02 ± 3.90	NA	NA	1979088	0.081	0.007	0.012*
Multimodal	Spos_7	22.06 ± 4.18	21.52 ± 4.14	NA	NA	2025673	0.130	<0.001	<0.001*
Multimodal	Spos_8	18.85 ± 4.57	18.97 ± 4.63	NA	NA	1861636	-0.025	0.506	0.589
Multimodal	Spos_9	19.43 ± 3.93	18.89 ± 3.71	NA	NA	2030350	0.141	<0.001	<0.001*
Multimodal	Spos_10	24.81 ± 3.73	24.69 ± 3.75	NA	NA	1920893	0.033	0.302	0.381
Multimodal	Spos_11	31.46 ± 3.59	31.05 ± 3.51	NA	NA	2014919	0.116	<0.001	<0.001*
Multimodal	Spos_12	27.49 ± 3.37	27.34 ± 3.47	NA	NA	1.436566	0.046	0.151	0.212
Multimodal	Spos_13	22.60 ± 3.84	22.11 ± 3.83	NA	NA	2032476	0.128	<0.001	<0.001*
Multimodal	Spos_14	19.74 ± 4.14	19.90 ± 3.97	NA	NA	1842201	-0.041	0.222	0.297

Multimodal	Spos_15	20.07 ± 3.83	19.64 ± 3.87	NA	NA	2001396	0.114	<0.001	0.002*
Multimodal	Spos_16	12.36 ± 4.38	12.46 ± 4.36	NA	NA	1862712	-0.022	0.526	0.607
Multimodal	Spos_17	14.18 ± 3.66	13.98 ± 3.56	NA	NA	1938409	0.053	0.125	0.178
Multimodal	Spos_18	23.74 ± 3.96	23.14 ± 3.79	NA	NA	2037417	0.154	<0.001	<0.001*
Multimodal	Spos_19	22.60 ± 3.65	22.21 ± 3.57	NA	NA	3.331856	0.107	<0.001	0.002*
Multimodal	Spos_20	13.78 ± 3.59	13.54 ± 3.56	NA	NA	1954499	0.066	0.046	0.070
Multimodal	Spos_21	23.41 ± 3.88	23.02 ± 3.93	NA	NA	1981651	0.102	0.006	0.010*
Multimodal	Spos_22	18.68 ± 3.98	18.21 ± 4.08	NA	NA	2010473	0.117	<0.001	<0.001*
Multimodal	Spos_23	11.91 ± 3.33	11.66 ± 3.21	NA	NA	1962385	0.076	0.027	0.042*
Multimodal	Spos_24	31.54 ± 4.01	31.59 ± 3.92	NA	NA	1861304	-0.014	0.500	0.587
Multimodal	Spos_25	24.96 ± 4.02	24.30 ± 4.07	NA	NA	2052941	0.163	<0.001	<0.001*
Multimodal	Spos_26	22.93 ± 3.41	22.87 ± 3.40	NA	NA	1898448	0.018	0.697	0.751
Multimodal	Spos_27	19.16 ± 4.48	18.71 ± 4.32	NA	NA	1981415	0.102	0.006	0.010*
Multimodal	Spos_28	19.94 ± 3.68	19.61 ± 3.63	NA	NA	1969331	0.091	0.016	0.026*
Multimodal	Spos_29	27.50 ± 3.87	27.22 ± 3.83	NA	NA	1968741	0.072	0.016	0.027*
Multimodal	Spos_30	12.59 ± 3.62	12.73 ± 3.75	NA	NA	1854541	-0.039	0.386	0.469
Multimodal	Spos_31	28.19 ± 4.09	27.46 ± 4.11	NA	NA	2085607	0.179	<0.001	<0.001*
Multimodal	Spos_32	14.11 ± 3.75	13.85 ± 3.76	NA	NA	1959673	0.068	0.032	0.050*
Multimodal	Spos_33	21.83 ± 3.74	21.29 ± 3.61	NA	NA	2024886	0.147	<0.001	<0.001*
Multimodal	Spos_34	18.28 ± 3.33	18.32 ± 3.28	NA	NA	1868616	-0.014	0.642	0.710
Multimodal	Spos_35	17.49 ± 3.94	17.27 ± 3.83	NA	NA	1954230	0.056	0.047	0.071
Multimodal	Spos_36	23.81 ± 3.66	24.17 ± 3.68	NA	NA	1766961	-0.097	<0.001	0.001*
Multimodal	Spos_37	27.78 ± 4.22	27.17 ± 4.15	NA	NA	2034651	0.147	<0.001	<0.001*
Multimodal	Spos_38	12.60 ± 3.61	12.17 ± 3.47	NA	NA	2016411	0.122	<0.001	<0.001*
Multimodal	Spos_39	31.57 ± 3.84	31.62 ± 3.61	NA	NA	1860531	-0.012	0.486	0.574
Multimodal	Spos_40	19.08 ± 3.97	18.73 ± 3.90	NA	NA	1972891	0.090	0.012	0.019*
Multimodal	Spos_41	19.33 ± 4.43	19.22 ± 4.45	NA	NA	1920421	0.025	0.309	0.386
Multimodal	Spos_42	19.07 ± 3.75	18.83 ± 3.79	NA	NA	1955040	0.063	0.045	0.068
Multimodal	Spos_43	9.56 ± 2.72	9.34 ± 2.64	NA	NA	1967589	0.082	0.018	0.029*
Multimodal	Spos_44	23.99 ± 3.98	23.25 ± 3.94	NA	NA	5.866091	0.188	<0.001	<0.001*
Multimodal	Spos_45	21.45 ± 4.05	20.99 ± 4.13	NA	NA	2011318	0.112	<0.001	<0.001*
Multimodal	Spos_46	17.29 ± 4.35	16.90 ± 4.09	NA	NA	1976560	0.092	0.009	0.014*
Multimodal	Spos_47	22.75 ± 4.48	22.09 ± 4.40	NA	NA	2039558	0.149	<0.001	<0.001*
Multimodal	Spos_48	22.33 ± 3.67	22.31 ± 3.64	NA	NA	1883918	0.005	0.979	0.982
Multimodal	Spos_49	30.02 ± 4.31	29.95 ± 4.34	NA	NA	0.483752	0.016	0.629	0.701

Multimodal	Spos_50	11.81 ± 3.03	11.48 ± 2.99	NA	NA	1995738	0.109	0.002	0.003*
Multimodal	Spos_51	12.05 ± 3.18	11.80 ± 2.96	NA	NA	1956628	0.080	0.040	0.061
Multimodal	Spos_52	12.58 ± 3.02	12.21 ± 2.98	NA	NA	2019557	0.123	<0.001	<0.001*
Multimodal	Spos_53	13.97 ± 3.85	13.53 ± 3.68	NA	NA	2005881	0.118	<0.001	<0.001*
Multimodal	Spos_54	11.76 ± 3.03	11.55 ± 2.91	NA	NA	1954886	0.070	0.045	0.068
Multimodal	Spos_55	9.76 ± 2.12	9.52 ± 2.09	NA	NA	1997646	0.116	0.001	0.002*
Multimodal	Sneg_1	18.53 ± 5.88	18.93 ± 5.92	NA	NA	1812413	-0.067	0.038	0.059
Multimodal	Sneg_2	28.59 ± 4.31	28.68 ± 4.15	NA	NA	-0.68871	-0.022	0.491	0.578
Multimodal	Sneg_3	19.15 ± 4.61	18.92 ± 4.42	NA	NA	1934897	0.051	0.152	0.213
Multimodal	Sneg_4	28.28 ± 6.29	28.61 ± 6.30	NA	NA	1831775	-0.052	0.129	0.182
Multimodal	Sneg_5	29.37 ± 4.37	29.57 ± 4.71	NA	NA	1835991	-0.043	0.162	0.224
Multimodal	Sneg_6	20.26 ± 7.12	20.12 ± 7.35	NA	NA	1912661	0.019	0.426	0.514
Multimodal	Sneg_7	23.10 ± 4.22	22.97 ± 4.23	NA	NA	1918441	0.031	0.337	0.415
Multimodal	Sneg_8	19.64 ± 6.46	19.34 ± 6.40	NA	NA	1938681	0.047	0.124	0.176
Multimodal	Sneg_9	19.95 ± 4.16	19.96 ± 4.01	NA	NA	1874214	-0.002	0.761	0.810
Multimodal	Sneg_10	25.80 ± 4.85	25.80 ± 5.01	NA	NA	1890530	0.001	0.871	0.909
Multimodal	Sneg_11	27.53 ± 4.08	27.41 ± 4.13	NA	NA	0.956622	0.031	0.339	0.417
Multimodal	Sneg_12	31.11 ± 4.74	31.03 ± 4.97	NA	NA	1911195	0.016	0.451	0.538
Multimodal	Sneg_13	22.70 ± 4.10	22.30 ± 3.91	NA	NA	1982656	0.099	0.005	0.009*
Multimodal	Sneg_14	24.16 ± 5.60	24.29 ± 5.71	NA	NA	1852379	-0.024	0.353	0.433
Multimodal	Sneg_15	23.56 ± 4.50	22.88 ± 4.27	NA	NA	2034255	0.154	<0.001	<0.001*
Multimodal	Sneg_16	14.71 ± 6.54	14.99 ± 6.66	NA	NA	1849301	-0.041	0.309	0.386
Multimodal	Sneg_17	19.16 ± 3.76	18.49 ± 3.62	NA	NA	2066576	0.181	<0.001	<0.001*
Multimodal	Sneg_18	26.88 ± 4.93	26.86 ± 4.92	NA	NA	1885276	0.003	0.990	0.992
Multimodal	Sneg_19	24.62 ± 5.14	24.33 ± 5.19	NA	NA	1937854	0.057	0.129	0.183
Multimodal	Sneg_20	19.17 ± 5.95	19.38 ± 5.96	NA	NA	1846370	-0.035	0.271	0.348
Multimodal	Sneg_21	21.66 ± 4.40	21.32 ± 4.42	NA	NA	1979291	0.078	0.007	0.012*
Multimodal	Sneg_22	18.32 ± 4.34	18.05 ± 4.37	NA	NA	1957865	0.064	0.037	0.057
Multimodal	Sneg_23	16.95 ± 3.74	16.63 ± 3.68	NA	NA	1970340	0.086	0.014	0.024*
Multimodal	Sneg_24	28.37 ± 4.18	28.63 ± 4.24	NA	NA	1802148	-0.062	0.018	0.029*
Multimodal	Sneg_25	22.29 ± 4.34	22.26 ± 4.35	NA	NA	1899885	0.008	0.667	0.726
Multimodal	Sneg_26	25.68 ± 4.40	25.76 ± 4.61	NA	NA	1869801	-0.017	0.667	0.726
Multimodal	Sneg_27	22.02 ± 4.04	21.71 ± 3.92	NA	NA	1955566	0.076	0.043	0.066
Multimodal	Sneg_28	22.18 ± 5.50	21.67 ± 5.45	NA	NA	1990324	0.093	0.003	0.004*
Multimodal	Sneg_29	23.59 ± 4.83	23.64 ± 4.75	NA	NA	1867432	-0.011	0.618	0.694

Multimodal	Sneg_30	16.93 ± 5.44	17.14 ± 5.47	NA	NA	1842710	-0.039	0.228	0.302
Multimodal	Sneg_31	25.13 ± 4.48	25.08 ± 4.46	NA	NA	1886527	0.010	0.962	0.969
Multimodal	Sneg_32	16.75 ± 5.67	16.86 ± 5.94	NA	NA	1877045	-0.019	0.823	0.868
Multimodal	Sneg_33	22.57 ± 4.62	22.37 ± 4.47	NA	NA	1931508	0.045	0.182	0.247
Multimodal	Sneg_34	25.10 ± 4.77	25.11 ± 4.58	NA	NA	1877232	-0.002	0.827	0.869
Multimodal	Sneg_35	18.52 ± 3.71	18.39 ± 3.79	NA	NA	1920233	0.033	0.311	0.388
Multimodal	Sneg_36	25.16 ± 4.20	25.12 ± 4.20	NA	NA	1888890	0.010	0.908	0.940
Multimodal	Sneg_37	25.24 ± 4.51	24.87 ± 4.49	NA	NA	2.602524	0.084	0.009	0.015*
Multimodal	Sneg_38	13.22 ± 3.35	12.95 ± 3.07	NA	NA	1965362	0.084	0.021	0.034*
Multimodal	Sneg_39	27.86 ± 5.01	28.30 ± 4.92	NA	NA	1799491	-0.087	0.015	0.024*
Multimodal	Sneg_40	22.55 ± 3.86	22.25 ± 3.87	NA	NA	1962254	0.077	0.027	0.042*
Multimodal	Sneg_41	19.43 ± 5.47	19.68 ± 5.52	NA	NA	1843798	-0.045	0.240	0.316
Multimodal	Sneg_42	21.69 ± 4.14	21.79 ± 4.14	NA	NA	1858103	-0.025	0.444	0.532
Multimodal	Sneg_43	16.84 ± 3.82	16.39 ± 3.76	NA	NA	2017867	0.118	<0.001	<0.001*
Multimodal	Sneg_44	22.69 ± 3.91	22.17 ± 3.95	NA	NA	2030701	0.130	<0.001	<0.001*
Multimodal	Sneg_45	18.54 ± 3.73	18.37 ± 3.73	NA	NA	1933688	0.046	0.162	0.224
Multimodal	Sneg_46	18.72 ± 3.59	18.65 ± 3.49	NA	NA	1892295	0.018	0.831	0.871
Multimodal	Sneg_47	17.08 ± 4.01	16.86 ± 4.05	NA	NA	1950079	0.055	0.062	0.092
Multimodal	Sneg_48	20.90 ± 4.25	20.73 ± 4.35	NA	NA	1921100	0.039	0.300	0.381
Multimodal	Sneg_49	19.71 ± 4.01	19.77 ± 3.87	NA	NA	1856251	-0.014	0.413	0.499
Multimodal	Sneg_50	16.21 ± 3.49	16.07 ± 3.28	NA	NA	1902101	0.041	0.622	0.696
Multimodal	Sneg_51	17.47 ± 3.60	17.43 ± 3.65	NA	NA	1903719	0.010	0.589	0.670
Multimodal	Sneg_52	16.62 ± 3.46	16.45 ± 3.44	NA	NA	1939947	0.047	0.115	0.164
Multimodal	Sneg_53	14.10 ± 4.18	14.21 ± 4.14	NA	NA	1835992	-0.028	0.162	0.224
Multimodal	Sneg_54	15.44 ± 3.61	15.12 ± 3.71	NA	NA	1996768	0.089	0.001	0.002*
Multimodal	Sneg_55	10.76 ± 2.03	10.92 ± 2.05	NA	NA	1809633	-0.078	0.031	0.049*
Multimodal	ADHD Demontis2022	0.28 ± 0.55	0.29 ± 0.55	NA	NA	-0.47828	-0.015	0.632	0.702
Multimodal	ALCDEP Walters2018	-1.15 ± 0.19	-1.14 ± 0.20	NA	NA	1837776	-0.049	0.178	0.243
Multimodal	AN Watson2019	-4.37 ± 0.59	-4.35 ± 0.61	NA	NA	1861535	-0.030	0.505	0.589
Multimodal	ASD Grove2019	-0.36 ± 0.35	-0.36 ± 0.35	NA	NA	0.068797	0.002	0.945	0.964
Multimodal	BD PGC4 2025	-1.46 ± 0.56	-1.46 ± 0.57	NA	NA	-0.27997	-0.009	0.780	0.825
Multimodal	BMI Locke2015	0.32 ± 0.21	0.32 ± 0.21	NA	NA	-0.45874	-0.015	0.646	0.713
Multimodal	bNGF Konieczny2025	-0.01 ± 0.04	-0.01 ± 0.04	NA	NA	-0.55099	-0.018	0.582	0.664
Multimodal	CAD Nikpay2015	0.91 ± 0.38	0.92 ± 0.40	NA	NA	-0.45707	-0.015	0.648	0.713
Multimodal	CCL11 Konieczny2025	-0.78 ± 0.26	-0.77 ± 0.27	NA	NA	1888136	-0.011	0.925	0.949

Multimodal	CCL2 Konieczny2025	0.27 ± 0.55	0.27 ± 0.55	NA	NA	1898610	0.005	0.694	0.748
Multimodal	CCL3 Konieczny2025	-0.46 ± 0.32	-0.45 ± 0.32	NA	NA	1836686	-0.048	0.168	0.231
Multimodal	CCL4 Konieczny2025	0.55 ± 0.41	0.55 ± 0.40	NA	NA	1883253	-0.012	0.963	0.969
Multimodal	CCL7 Konieczny2025	-0.95 ± 0.38	-0.94 ± 0.39	NA	NA	1849184	-0.017	0.307	0.386
Multimodal	CRP Said2022	0.27 ± 0.39	0.29 ± 0.40	NA	NA	-1.35608	-0.044	0.175	0.239
Multimodal	CSF1 Konieczny2025	0.70 ± 0.64	0.70 ± 0.65	NA	NA	-0.12524	-0.004	0.900	0.934
Multimodal	CSF3 Konieczny2025	0.48 ± 0.30	0.46 ± 0.30	NA	NA	1925896	0.041	0.240	0.316
Multimodal	CTACK Konieczny2025	-0.04 ± 0.05	-0.04 ± 0.05	NA	NA	1858946	-0.024	0.458	0.545
Multimodal	CUD Johnson2020	-1.13 ± 0.32	-1.12 ± 0.32	NA	NA	1870075	-0.020	0.672	0.728
Multimodal	CXCL1 Konieczny2025	-3.37 ± 0.72	-3.38 ± 0.75	NA	NA	1895188	0.017	0.767	0.814
Multimodal	CXCL10 Konieczny2025	-0.10 ± 0.11	-0.10 ± 0.10	NA	NA	0.92819	0.030	0.353	0.433
Multimodal	CXCL12 Konieczny2025	0.17 ± 0.13	0.17 ± 0.13	NA	NA	-0.05826	-0.002	0.954	0.969
Multimodal	CXCL9 Konieczny2025	-0.02 ± 0.09	-0.02 ± 0.09	NA	NA	-1.00346	-0.032	0.316	0.392
Multimodal	FGFb Konieczny2025	0.54 ± 0.37	0.53 ± 0.38	NA	NA	1888437	0.016	0.918	0.946
Multimodal	GAD FinnGen2024	0.13 ± 0.29	0.14 ± 0.30	NA	NA	-1.07275	-0.034	0.283	0.363
Multimodal	HbA1c Willems2023	0.12 ± 0.07	0.12 ± 0.07	NA	NA	-0.12942	-0.004	0.897	0.933
Multimodal	HDL Graham2021	1.89 ± 0.42	1.89 ± 0.44	NA	NA	1869070	-0.011	0.652	0.713
Multimodal	HGF Konieczny2025	0.36 ± 0.12	0.36 ± 0.12	NA	NA	1883215	-0.012	0.963	0.969
Multimodal	IFNg Konieczny2025	0.11 ± 0.10	0.11 ± 0.10	NA	NA	1887605	0.013	0.937	0.957
Multimodal	IL10 Konieczny2025	0.04 ± 0.05	0.04 ± 0.05	NA	NA	-1.12846	-0.036	0.259	0.337
Multimodal	IL13 Konieczny2025	-0.01 ± 0.09	-0.01 ± 0.10	NA	NA	1848874	-0.032	0.303	0.381
Multimodal	IL16 Konieczny2025	0.28 ± 0.44	0.29 ± 0.48	NA	NA	1869132	-0.022	0.653	0.713
Multimodal	IL17 Konieczny2025	0.06 ± 0.05	0.06 ± 0.04	NA	NA	-1.27974	-0.041	0.201	0.271
Multimodal	IL18 Konieczny2025	1.31 ± 1.09	1.25 ± 1.12	NA	NA	1948151	0.059	0.070	0.103
Multimodal	IL1b Konieczny2025	-0.78 ± 0.17	-0.77 ± 0.17	NA	NA	1817470	-0.056	0.054	0.080
Multimodal	IL1RA Konieczny2025	-0.30 ± 0.17	-0.31 ± 0.17	NA	NA	1.775911	0.057	0.076	0.111
Multimodal	IL2 Konieczny2025	0.18 ± 0.07	0.17 ± 0.07	NA	NA	1.684669	0.054	0.092	0.134
Multimodal	IL2RA Konieczny2025	0.08 ± 0.07	0.08 ± 0.07	NA	NA	1847716	-0.029	0.288	0.367
Multimodal	IL4 Konieczny2025	0.06 ± 0.05	0.06 ± 0.05	NA	NA	1896821	0.004	0.732	0.783
Multimodal	IL5 Konieczny2025	0.08 ± 0.05	0.09 ± 0.05	NA	NA	-0.45418	-0.015	0.650	0.713
Multimodal	IL6 Konieczny2025	0.08 ± 0.06	0.08 ± 0.06	NA	NA	1842315	-0.038	0.224	0.298
Multimodal	IL7 Konieczny2025	-0.02 ± 0.04	-0.02 ± 0.04	NA	NA	-1.11023	-0.036	0.267	0.345
Multimodal	IL8 Konieczny2025	0.15 ± 0.09	0.15 ± 0.09	NA	NA	-0.5408	-0.017	0.589	0.670
Multimodal	IL9 Konieczny2025	0.12 ± 0.09	0.12 ± 0.08	NA	NA	-0.61542	-0.020	0.538	0.619
Multimodal	LDL Graham2021	0.31 ± 0.40	0.32 ± 0.41	NA	NA	1865206	-0.012	0.574	0.657

Multimodal	MDD PGC4 2025	-0.92 ± 0.36	-0.90 ± 0.37	NA	NA	1868979	-0.034	0.650	0.713
Multimodal	MIF Konieczny2025	0.03 ± 0.05	0.03 ± 0.04	NA	NA	1960543	0.066	0.030	0.047*
Multimodal	NEUROT DeMoor2015	-0.15 ± 0.05	-0.15 ± 0.05	NA	NA	0.305421	0.010	0.760	0.810
Multimodal	OCD PGC3 2018	-0.03 ± 0.32	-0.05 ± 0.32	NA	NA	1947532	0.047	0.073	0.107
Multimodal	PDGFBB Konieczny2025	0.20 ± 0.16	0.20 ± 0.16	NA	NA	0.417596	0.013	0.676	0.731
Multimodal	PTSD Nievergelt2024	-0.45 ± 0.28	-0.44 ± 0.30	NA	NA	1863912	-0.029	0.549	0.630
Multimodal	RANTES Konieczny2025	0.19 ± 0.17	0.18 ± 0.18	NA	NA	1960992	0.070	0.029	0.046*
Multimodal	SCF Konieczny2025	0.85 ± 0.23	0.85 ± 0.23	NA	NA	0.67112	0.022	0.502	0.588
Multimodal	SCGFb Konieczny2025	-0.04 ± 0.25	-0.04 ± 0.24	NA	NA	1899818	0.007	0.669	0.726
Multimodal	SCZ Trubetsky2022	-5.17 ± 1.05	-5.12 ± 1.09	NA	NA	1836857	-0.043	0.170	0.232
Multimodal	T2D Verma2024	-12.54 ± 0.91	-12.54 ± 1.03	NA	NA	1924361	-0.002	0.258	0.336
Multimodal	TNFa Konieczny2025	0.07 ± 0.04	0.07 ± 0.04	NA	NA	-0.51022	-0.016	0.610	0.688
Multimodal	TNFb Konieczny2025	0.06 ± 0.05	0.06 ± 0.05	NA	NA	-1.10547	-0.035	0.269	0.347
Multimodal	TRAIL Konieczny2025	-0.27 ± 0.35	-0.26 ± 0.35	NA	NA	1889747	-0.004	0.889	0.926
Multimodal	TRIG Graham2021	-1.47 ± 0.38	-1.48 ± 0.38	NA	NA	1911975	0.024	0.438	0.525
Multimodal	VEGF Konieczny2025	-0.60 ± 0.29	-0.60 ± 0.29	NA	NA	1876904	-0.008	0.820	0.867

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; DTI, diffusion tensor imaging; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; fMRI, functional magnetic resonance imaging; GM, grey matter; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NA, not applicable; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; rs-fMRI, resting-state fMRI; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; t-fMRI, task-based fMRI; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Table A6. Input feature comparisons between clusters resulting from the significant stratification models among the dMDD sample of the UKB dataset.

Model	Variable	C10	C11	Statistic	Effect size	p-value	q-value
GM	Area of caudalanteriorcingulate L	1031.42 ± 166.29	1075.86 ± 185.87	8538.5	-0.251	0.079	0.119
GM	Area of caudalanteriorcingulate R	727.48 ± 128.58	778.80 ± 182.53	8020	-0.323	0.011	0.022*
GM	Area of caudalmiddlefrontal L	2299.04 ± 321.23	2369.49 ± 375.86	8862	-0.201	0.201	0.261
GM	Area of caudalmiddlefrontal R	2134.40 ± 344.01	2202.33 ± 355.19	8613	-0.194	0.099	0.144
GM	Area of cuneus L	2083.35 ± 281.77	2052.49 ± 285.86	10203.5	0.108	0.477	0.533
GM	Area of cuneus R	1984.63 ± 268.42	1971.10 ± 252.11	9996	0.052	0.687	0.716
GM	Area of entorhinal L	407.90 ± 74.27	409.94 ± 77.05	9625	-0.027	0.884	0.900
GM	Area of entorhinal R	366.12 ± 62.59	368.09 ± 73.29	9735	-0.029	0.988	0.988
GM	Area of fusiform L	2752.09 ± 335.15	2804.97 ± 343.94	9069.5	-0.155	0.332	0.392
GM	Area of fusiform R	2717.96 ± 340.20	2774.27 ± 368.68	8973.5	-0.158	0.266	0.328
GM	Area of inferiorparietal L	4178.59 ± 569.81	4281.33 ± 568.56	8494.5	-0.180	0.068	0.106
GM	Area of inferiorparietal R	4846.27 ± 657.84	5049.40 ± 665.63	7956	-0.306	0.009	0.018*
GM	Area of inferiortemporal L	3320.29 ± 437.26	3370.37 ± 417.39	8871	-0.117	0.206	0.265
GM	Area of inferiortemporal R	3466.59 ± 446.63	3591.10 ± 455.80	8134	-0.275	0.018	0.033*
GM	Area of insula L	1929.10 ± 188.65	1957.78 ± 201.37	8742.5	-0.146	0.145	0.200
GM	Area of insula R	2018.68 ± 194.22	2057.55 ± 209.59	-1.60485	-0.192	0.110	0.156
GM	Area of isthmuscingulate L	991.40 ± 127.84	1003.62 ± 182.95	9522.5	-0.077	0.765	0.789
GM	Area of isthmuscingulate R	880.84 ± 135.21	884.00 ± 147.43	9561	-0.022	0.809	0.830
GM	Area of lateraloccipital L	4933.15 ± 556.64	5042.08 ± 637.95	8916	-0.181	0.231	0.292
GM	Area of lateraloccipital R	4965.90 ± 604.96	5095.36 ± 697.15	8831.5	-0.197	0.185	0.247
GM	Area of lateralorbitofrontal L	2889.43 ± 284.95	2921.68 ± 315.40	-0.89455	-0.107	0.372	0.432
GM	Area of lateralorbitofrontal R	2904.96 ± 298.93	2939.10 ± 350.93	-0.8729	-0.104	0.383	0.441
GM	Area of lingual L	3131.82 ± 390.05	3110.15 ± 397.80	0.459288	0.055	0.646	0.684
GM	Area of lingual R	3187.70 ± 402.82	3184.06 ± 434.99	10090	0.009	0.587	0.632
GM	Area of medialorbitofrontal L	1539.95 ± 168.49	1585.20 ± 173.68	-2.20701	-0.264	0.028	0.049*
GM	Area of medialorbitofrontal R	1463.92 ± 168.26	1507.01 ± 171.62	8335.5	-0.253	0.039	0.066
GM	Area of middletemporal L	4026.23 ± 487.07	4159.76 ± 553.80	8445	-0.255	0.058	0.093
GM	Area of middletemporal R	3994.59 ± 437.19	4150.84 ± 506.62	8057	-0.329	0.013	0.025*
GM	Area of paracentral L	1547.66 ± 186.15	1589.78 ± 213.09	8494.5	-0.210	0.068	0.106
GM	Area of paracentral R	1529.10 ± 187.79	1581.30 ± 204.59	8261.5	-0.265	0.030	0.052
GM	Area of parahippocampal L	685.82 ± 77.70	689.09 ± 76.98	9430.5	-0.042	0.664	0.699
GM	Area of parahippocampal R	665.18 ± 69.17	672.22 ± 73.17	9325	-0.099	0.554	0.606

GM	Area of parsopercularis L	1404.24 ± 198.13	1426.57 ± 218.11	9103	-0.107	0.357	0.418
GM	Area of parsopercularis R	1508.57 ± 214.76	1548.52 ± 237.91	8669	-0.176	0.117	0.164
GM	Area of parsorbitalis L	660.64 ± 75.49	668.12 ± 87.68	9449.5	-0.091	0.684	0.716
GM	Area of parsorbitalis R	680.44 ± 94.03	697.31 ± 108.18	8765	-0.166	0.155	0.212
GM	Area of parstriangularis L	1523.12 ± 200.75	1559.53 ± 268.08	9369	-0.153	0.599	0.637
GM	Area of parstriangularis R	1439.09 ± 221.41	1449.83 ± 221.86	9283.5	-0.048	0.514	0.568
GM	Area of pericalcarine L	1419.54 ± 252.42	1358.11 ± 245.62	10999.5	0.246	0.058	0.093
GM	Area of pericalcarine R	1542.89 ± 277.35	1503.43 ± 261.42	1.223237	0.146	0.222	0.285
GM	Area of postcentral L	4486.35 ± 439.32	4622.00 ± 514.26	8182	-0.282	0.022	0.039*
GM	Area of postcentral R	4227.47 ± 478.30	4398.45 ± 561.84	7926	-0.326	0.008	0.016*
GM	Area of posteriorcingulate L	1218.52 ± 165.66	1253.13 ± 193.51	8848.5	-0.191	0.194	0.256
GM	Area of posteriorcingulate R	1165.79 ± 143.75	1208.54 ± 178.54	8324	-0.262	0.038	0.064
GM	Area of precentral L	4574.22 ± 478.81	4648.92 ± 513.03	8787.5	-0.150	0.165	0.224
GM	Area of precentral R	4420.10 ± 499.97	4510.90 ± 543.99	8601.5	-0.173	0.096	0.140
GM	Area of precuneus L	3552.40 ± 392.67	3677.86 ± 486.07	8522.5	-0.282	0.075	0.115
GM	Area of precuneus R	3933.10 ± 533.72	4000.63 ± 531.97	8989	-0.126	0.276	0.336
GM	Area of rostralanteriorcingulate L	1139.88 ± 194.64	1163.90 ± 212.13	9364.5	-0.118	0.594	0.635
GM	Area of rostralanteriorcingulate R	781.69 ± 143.28	804.08 ± 171.42	9068	-0.141	0.331	0.392
GM	Area of rostralmiddlefrontal L	3863.66 ± 527.92	3925.82 ± 580.13	9170	-0.112	0.411	0.465
GM	Area of rostralmiddlefrontal R	3999.68 ± 517.15	4067.46 ± 618.80	9345	-0.118	0.574	0.624
GM	Area of superiorfrontal L	7502.96 ± 831.56	7719.84 ± 965.16	8584	-0.240	0.091	0.134
GM	Area of superiorfrontal R	8618.91 ± 975.84	8774.87 ± 1032.93	8943.5	-0.155	0.247	0.307
GM	Area of superiorparietal L	4128.31 ± 513.00	4328.60 ± 582.33	-3.04246	-0.363	0.003	0.006*
GM	Area of superiorparietal R	4240.54 ± 556.52	4405.24 ± 594.91	-2.38515	-0.285	0.018	0.032*
GM	Area of superiortemporal L	4963.85 ± 532.61	5014.89 ± 563.59	9005	-0.093	0.286	0.345
GM	Area of superiortemporal R	4660.06 ± 445.20	4705.73 ± 513.42	9256.5	-0.095	0.488	0.542
GM	Area of supramarginal L	3506.76 ± 563.91	3578.52 ± 563.65	8855	-0.127	0.197	0.258
GM	Area of supramarginal R	3343.10 ± 442.45	3408.27 ± 484.57	-1.17134	-0.140	0.242	0.303
GM	Area of transversetemporal L	452.60 ± 70.98	449.13 ± 79.50	10208.5	0.046	0.472	0.531
GM	Area of transversetemporal R	326.15 ± 48.33	332.65 ± 51.34	8982.5	-0.130	0.271	0.333
GM	Volume of caudalanteriorcingulate L	3068.26 ± 582.73	3090.72 ± 604.23	9771	-0.038	0.945	0.955
GM	Volume of caudalanteriorcingulate R	2206.32 ± 475.02	2230.48 ± 576.15	9627	-0.046	0.886	0.900
GM	Volume of caudalmiddlefrontal L	7309.56 ± 1065.20	7016.16 ± 1145.30	11540.5	0.264	0.007	0.015*
GM	Volume of caudalmiddlefrontal R	6733.36 ± 1116.26	6512.41 ± 1112.48	10862	0.198	0.091	0.134
GM	Volume of cuneus L	4563.03 ± 744.50	4154.94 ± 649.50	12768.5	0.584	<0.001	<0.001*

GM	Volume of cuneus R	4076.24 ± 652.31	3729.38 ± 528.26	12968.5	0.584	<0.001	<0.001*
GM	Volume of entorhinal L	1775.51 ± 333.41	1691.80 ± 341.92	11395	0.247	0.013	0.025*
GM	Volume of entorhinal R	1704.45 ± 256.59	1594.27 ± 306.91	12224	0.388	<0.001	<0.001*
GM	Volume of fusiform L	9150.65 ± 1210.70	8873.64 ± 1151.09	11096.5	0.234	0.042	0.068
GM	Volume of fusiform R	9138.60 ± 1197.65	8750.03 ± 1180.55	11578.5	0.326	0.006	0.013*
GM	Volume of inferiorparietal L	12589.62 ± 1806.75	12200.75 ± 1688.76	1.858154	0.222	0.064	0.102
GM	Volume of inferiorparietal R	14972.36 ± 2086.10	14586.05 ± 1933.45	10544	0.192	0.224	0.285
GM	Volume of inferiortemporal L	12668.54 ± 1724.21	12244.91 ± 1588.55	11122	0.255	0.038	0.064
GM	Volume of inferiortemporal R	12833.78 ± 1714.33	12447.92 ± 1678.34	11014	0.227	0.056	0.090
GM	Volume of insula L	6340.38 ± 616.46	6125.07 ± 661.70	11679	0.335	0.004	0.008*
GM	Volume of insula R	6638.61 ± 666.00	6362.40 ± 695.32	12244.5	0.404	<0.001	<0.001*
GM	Volume of isthmuscingulate L	2743.93 ± 340.76	2650.90 ± 470.14	11210.5	0.225	0.027	0.048*
GM	Volume of isthmuscingulate R	2623.04 ± 405.18	2472.10 ± 403.22	11719.5	0.372	0.003	0.007*
GM	Volume of lateraloccipital L	12833.17 ± 1645.78	12284.03 ± 1680.93	2.755458	0.329	0.006	0.013*
GM	Volume of lateraloccipital R	13092.90 ± 1796.04	12440.43 ± 1766.41	11786.5	0.365	0.002	0.005*
GM	Volume of lateralorbitofrontal L	9249.47 ± 935.94	8845.12 ± 986.03	12243	0.419	<0.001	<0.001*
GM	Volume of lateralorbitofrontal R	9318.93 ± 887.44	8884.41 ± 969.13	12567.5	0.466	<0.001	<0.001*
GM	Volume of lingual L	6841.86 ± 1101.66	6357.03 ± 1082.37	3.707472	0.443	<0.001	<0.001*
GM	Volume of lingual R	6789.52 ± 1002.31	6368.59 ± 1026.55	12298	0.414	<0.001	<0.001*
GM	Volume of medialorbitofrontal L	5031.38 ± 638.61	4902.30 ± 550.44	1.811129	0.216	0.071	0.110
GM	Volume of medialorbitofrontal R	4888.97 ± 565.01	4783.24 ± 493.11	10906	0.199	0.079	0.119
GM	Volume of middletemporal L	14200.15 ± 1898.17	13878.59 ± 1937.17	10827	0.167	0.102	0.146
GM	Volume of middletemporal R	14385.04 ± 1710.65	13979.62 ± 1793.07	11111	0.231	0.040	0.066
GM	Volume of paracentral L	4723.34 ± 581.89	4445.66 ± 575.15	12340.5	0.479	<0.001	<0.001*
GM	Volume of paracentral R	4578.04 ± 548.29	4318.92 ± 579.08	12287	0.458	<0.001	<0.001*
GM	Volume of parahippocampal L	2239.30 ± 276.61	2087.60 ± 306.61	13073.5	0.517	<0.001	<0.001*
GM	Volume of parahippocampal R	2102.33 ± 219.03	1970.88 ± 239.37	12879.5	0.571	<0.001	<0.001*
GM	Volume of parsopercularis L	4633.19 ± 726.96	4422.54 ± 703.77	11432.5	0.294	0.011	0.022*
GM	Volume of parsopercularis R	4774.30 ± 712.08	4662.31 ± 747.32	10633.5	0.153	0.177	0.239
GM	Volume of parsorbitalis L	2282.21 ± 304.96	2183.86 ± 305.84	11701.5	0.321	0.003	0.007*
GM	Volume of parsorbitalis R	2371.30 ± 321.58	2267.10 ± 345.68	11458	0.311	0.010	0.020*
GM	Volume of parstriangularis L	4647.62 ± 645.81	4473.03 ± 793.73	11511.5	0.240	0.008	0.016*
GM	Volume of parstriangularis R	4330.42 ± 744.92	4056.76 ± 653.82	11688	0.390	0.004	0.008*
GM	Volume of pericalcarine L	2203.79 ± 451.46	2016.58 ± 414.44	12055.5	0.431	<0.001	0.001*
GM	Volume of pericalcarine R	2340.25 ± 468.84	2190.29 ± 425.70	2.799475	0.334	0.005	0.012*

GM	Volume of postcentral L	11896.33 ± 1310.52	11333.20 ± 1399.46	3.465073	0.414	<0.001	0.002*
GM	Volume of postcentral R	11177.64 ± 1315.12	10660.48 ± 1546.73	11970.5	0.359	<0.001	0.002*
GM	Volume of posteriorcingulate L	3591.66 ± 542.95	3530.19 ± 519.82	10300.5	0.115	0.393	0.449
GM	Volume of posteriorcingulate R	3617.37 ± 457.12	3547.36 ± 500.17	10433.5	0.146	0.293	0.350
GM	Volume of precentral L	14496.08 ± 1682.72	13598.05 ± 1668.14	4.475529	0.535	<0.001	<0.001*
GM	Volume of precentral R	13923.34 ± 1732.50	13022.44 ± 1754.39	12543.5	0.515	<0.001	<0.001*
GM	Volume of precuneus L	10522.26 ± 1155.55	10066.83 ± 1192.20	3.23747	0.387	0.001	0.003*
GM	Volume of precuneus R	11357.44 ± 1379.76	10720.10 ± 1337.20	12353.5	0.468	<0.001	<0.001*
GM	Volume of rostralanteriorcingulate L	3764.06 ± 669.99	3660.33 ± 668.94	10733	0.155	0.134	0.187
GM	Volume of rostralanteriorcingulate R	2699.07 ± 500.97	2602.99 ± 544.21	10920	0.183	0.076	0.116
GM	Volume of rostralmiddlefrontal L	11894.03 ± 1688.83	11403.57 ± 1815.00	11359.5	0.279	0.015	0.028*
GM	Volume of rostralmiddlefrontal R	12020.21 ± 1595.04	11567.64 ± 1792.22	11476.5	0.266	0.009	0.019*
GM	Volume of superiorfrontal L	25863.62 ± 2988.30	24941.62 ± 3070.57	11326.5	0.303	0.017	0.032*
GM	Volume of superiorfrontal R	28938.46 ± 3414.30	27707.21 ± 3184.08	11816	0.372	0.002	0.004*
GM	Volume of superiorparietal L	11568.75 ± 1493.46	11356.03 ± 1532.72	1.173248	0.140	0.242	0.303
GM	Volume of superiorparietal R	11871.01 ± 1557.05	11382.24 ± 1453.44	2.711768	0.324	0.007	0.015*
GM	Volume of superiortemporal L	17679.24 ± 1943.35	16778.08 ± 1955.95	12185.5	0.461	<0.001	<0.001*
GM	Volume of superiortemporal R	16945.03 ± 1615.85	15908.73 ± 1819.34	5.021002	0.600	<0.001	<0.001*
GM	Volume of supramarginal L	11012.97 ± 1741.16	10512.62 ± 1552.91	11109	0.303	0.040	0.066
GM	Volume of supramarginal R	10542.73 ± 1418.01	10003.94 ± 1423.15	3.166389	0.378	0.002	0.004*
GM	Volume of transversetemporal L	1315.12 ± 246.74	1183.65 ± 221.90	12902	0.560	<0.001	<0.001*
GM	Volume of transversetemporal R	1046.63 ± 169.19	952.10 ± 169.44	12871.5	0.557	<0.001	<0.001*
GM	Mean thickness of caudalanteriorcingulate L	2.79 ± 0.24	2.70 ± 0.29	11327.5	0.345	0.017	0.032*
GM	Mean thickness of caudalanteriorcingulate R	2.59 ± 0.32	2.49 ± 0.34	11429.5	0.291	0.011	0.022*
GM	Mean thickness of caudalmiddlefrontal L	2.95 ± 0.10	2.79 ± 0.13	11.0973	1.326	<0.001	<0.001*
GM	Mean thickness of caudalmiddlefrontal R	2.90 ± 0.11	2.75 ± 0.13	10.87983	1.300	<0.001	<0.001*
GM	Mean thickness of cuneus L	2.12 ± 0.12	1.98 ± 0.13	8.892238	1.062	<0.001	<0.001*
GM	Mean thickness of cuneus R	2.01 ± 0.13	1.89 ± 0.11	8.94564	1.069	<0.001	<0.001*
GM	Mean thickness of entorhinal L	3.33 ± 0.25	3.20 ± 0.28	4.015472	0.480	<0.001	<0.001*
GM	Mean thickness of entorhinal R	3.43 ± 0.26	3.24 ± 0.30	13488	0.660	<0.001	<0.001*
GM	Mean thickness of fusiform L	2.95 ± 0.10	2.83 ± 0.11	15019.5	1.073	<0.001	<0.001*
GM	Mean thickness of fusiform R	2.96 ± 0.10	2.82 ± 0.13	15611.5	1.205	<0.001	<0.001*
GM	Mean thickness of inferiorparietal L	2.77 ± 0.08	2.65 ± 0.09	16501	1.419	<0.001	<0.001*
GM	Mean thickness of inferiorparietal R	2.82 ± 0.09	2.67 ± 0.09	16898	1.561	<0.001	<0.001*
GM	Mean thickness of inferiortemporal L	3.12 ± 0.13	2.99 ± 0.13	8.219231	0.982	<0.001	<0.001*
GM	Mean thickness of inferiortemporal R	3.09 ± 0.11	2.94 ± 0.12	10.28588	1.229	<0.001	<0.001*

GM	Mean thickness of insula L	3.26 ± 0.13	3.12 ± 0.16	7.965128	0.951	<0.001	<0.001 *
GM	Mean thickness of insula R	3.28 ± 0.12	3.10 ± 0.14	10.77176	1.287	<0.001	<0.001 *
GM	Mean thickness of isthmuscingulate L	2.51 ± 0.17	2.44 ± 0.18	12253.5	0.433	<0.001	<0.001 *
GM	Mean thickness of isthmuscingulate R	2.60 ± 0.19	2.49 ± 0.18	13221.5	0.623	<0.001	<0.001 *
GM	Mean thickness of lateraloccipital L	2.38 ± 0.10	2.27 ± 0.11	8.510452	1.017	<0.001	<0.001 *
GM	Mean thickness of lateraloccipital R	2.42 ± 0.10	2.28 ± 0.11	16118	1.338	<0.001	<0.001 *
GM	Mean thickness of lateralorbitofrontal L	2.90 ± 0.13	2.77 ± 0.12	15221.5	1.070	<0.001	<0.001 *
GM	Mean thickness of lateralorbitofrontal R	2.89 ± 0.11	2.76 ± 0.12	9.167211	1.095	<0.001	<0.001 *
GM	Mean thickness of lingual L	2.08 ± 0.14	1.97 ± 0.14	6.579144	0.786	<0.001	<0.001 *
GM	Mean thickness of lingual R	2.06 ± 0.13	1.96 ± 0.13	6.618767	0.791	<0.001	<0.001 *
GM	Mean thickness of medialorbitofrontal L	2.70 ± 0.16	2.59 ± 0.16	5.790989	0.692	<0.001	<0.001 *
GM	Mean thickness of medialorbitofrontal R	2.73 ± 0.17	2.63 ± 0.17	5.022104	0.600	<0.001	<0.001 *
GM	Mean thickness of middletemporal L	2.96 ± 0.13	2.85 ± 0.14	14242.5	0.855	<0.001	<0.001 *
GM	Mean thickness of middletemporal R	3.07 ± 0.12	2.91 ± 0.13	10.11007	1.208	<0.001	<0.001 *
GM	Mean thickness of paracentral L	2.81 ± 0.15	2.62 ± 0.16	10.28318	1.228	<0.001	<0.001 *
GM	Mean thickness of paracentral R	2.80 ± 0.14	2.60 ± 0.15	11.91835	1.424	<0.001	<0.001 *
GM	Mean thickness of parahippocampal L	2.87 ± 0.27	2.70 ± 0.27	5.311749	0.634	<0.001	<0.001 *
GM	Mean thickness of parahippocampal R	2.79 ± 0.21	2.62 ± 0.22	6.442805	0.770	<0.001	<0.001 *
GM	Mean thickness of parsopercularis L	2.94 ± 0.12	2.81 ± 0.13	9.013633	1.077	<0.001	<0.001 *
GM	Mean thickness of parsopercularis R	2.88 ± 0.11	2.76 ± 0.12	8.766452	1.047	<0.001	<0.001 *
GM	Mean thickness of parsorbitalis L	2.95 ± 0.16	2.81 ± 0.14	14546	0.961	<0.001	<0.001 *
GM	Mean thickness of parsorbitalis R	2.97 ± 0.15	2.80 ± 0.16	8.913587	1.065	<0.001	<0.001 *
GM	Mean thickness of parstriangularis L	2.79 ± 0.12	2.65 ± 0.13	15335.5	1.118	<0.001	<0.001 *
GM	Mean thickness of parstriangularis R	2.76 ± 0.11	2.61 ± 0.10	11.77448	1.406	<0.001	<0.001 *
GM	Mean thickness of pericalcarine L	1.78 ± 0.13	1.71 ± 0.13	4.718978	0.564	<0.001	<0.001 *
GM	Mean thickness of pericalcarine R	1.74 ± 0.12	1.67 ± 0.14	4.385958	0.524	<0.001	<0.001 *
GM	Mean thickness of postcentral L	2.43 ± 0.10	2.28 ± 0.11	11.40127	1.362	<0.001	<0.001 *
GM	Mean thickness of postcentral R	2.40 ± 0.11	2.24 ± 0.13	16512.5	1.372	<0.001	<0.001 *
GM	Mean thickness of posteriorcingulate L	2.73 ± 0.16	2.64 ± 0.17	4.600827	0.550	<0.001	<0.001 *
GM	Mean thickness of posteriorcingulate R	2.75 ± 0.15	2.66 ± 0.17	5.0625	0.605	<0.001	<0.001 *
GM	Mean thickness of precentral L	2.94 ± 0.11	2.75 ± 0.14	16778	1.447	<0.001	<0.001 *
GM	Mean thickness of precentral R	2.89 ± 0.12	2.69 ± 0.15	16959.5	1.497	<0.001	<0.001 *
GM	Mean thickness of precuneus L	2.73 ± 0.10	2.56 ± 0.11	13.49355	1.612	<0.001	<0.001 *
GM	Mean thickness of precuneus R	2.72 ± 0.10	2.56 ± 0.10	13.10049	1.565	<0.001	<0.001 *
GM	Mean thickness of rostralanteriorcingulate L	2.95 ± 0.14	2.86 ± 0.18	12722.5	0.571	<0.001	<0.001 *
GM	Mean thickness of rostralanteriorcingulate R	3.02 ± 0.20	2.88 ± 0.19	13344	0.678	<0.001	<0.001 *

GM	Mean thickness of rostralmiddlefrontal L	2.75 ± 0.09	2.63 ± 0.11	15855.5	1.254	<0.001	<0.001*
GM	Mean thickness of rostralmiddlefrontal R	2.70 ± 0.08	2.58 ± 0.10	15884.5	1.250	<0.001	<0.001*
GM	Mean thickness of superiorfrontal L	3.04 ± 0.10	2.89 ± 0.12	16457.5	1.412	<0.001	<0.001*
GM	Mean thickness of superiorfrontal R	3.00 ± 0.08	2.85 ± 0.10	17131.5	1.580	<0.001	<0.001*
GM	Mean thickness of superiorparietal L	2.56 ± 0.10	2.42 ± 0.10	11.53249	1.378	<0.001	<0.001*
GM	Mean thickness of superiorparietal R	2.55 ± 0.10	2.39 ± 0.10	13.18194	1.575	<0.001	<0.001*
GM	Mean thickness of superiortemporal L	3.07 ± 0.11	2.92 ± 0.14	15600	1.178	<0.001	<0.001*
GM	Mean thickness of superiortemporal R	3.15 ± 0.13	2.98 ± 0.13	16106.5	1.315	<0.001	<0.001*
GM	Mean thickness of supramarginal L	2.90 ± 0.10	2.75 ± 0.10	12.06056	1.441	<0.001	<0.001*
GM	Mean thickness of supramarginal R	2.92 ± 0.11	2.75 ± 0.11	12.9418	1.546	<0.001	<0.001*
GM	Mean thickness of transversetemporal L	2.62 ± 0.22	2.43 ± 0.22	7.208535	0.861	<0.001	<0.001*
GM	Mean thickness of transversetemporal R	2.70 ± 0.25	2.48 ± 0.24	7.653356	0.914	<0.001	<0.001*
GM	Volume of accumbens L	519.76 ± 125.66	500.70 ± 115.85	10625.5	0.157	0.181	0.243
GM	Volume of accumbens R	422.33 ± 107.35	411.44 ± 100.66	0.874488	0.104	0.383	0.441
GM	Volume of amygdala L	1226.58 ± 222.79	1226.17 ± 220.00	0.015579	0.002	0.988	0.988
GM	Volume of amygdala R	1211.40 ± 263.58	1156.20 ± 236.23	10599	0.220	0.194	0.256
GM	Volume of caudate L	3396.35 ± 411.53	3320.85 ± 383.04	1.587068	0.190	0.114	0.160
GM	Volume of caudate R	3543.26 ± 410.31	3463.86 ± 398.96	1.638671	0.196	0.102	0.146
GM	Volume of hippocampus L	3872.56 ± 478.34	3759.00 ± 429.41	11290.5	0.249	0.020	0.036*
GM	Volume of hippocampus R	3957.14 ± 466.02	3861.90 ± 463.33	1.711295	0.204	0.088	0.132
GM	Volume of pallidum L	1738.01 ± 228.49	1722.91 ± 226.01	0.554768	0.066	0.580	0.626
GM	Volume of pallidum R	1795.76 ± 233.09	1769.97 ± 213.48	10157	0.115	0.521	0.572
GM	Volume of putamen L	4857.26 ± 565.91	4830.47 ± 561.84	0.39679	0.047	0.692	0.717
GM	Volume of putamen R	4919.30 ± 578.60	4845.45 ± 551.39	10365.5	0.130	0.341	0.402
GM	Volume of thalamus L	7804.74 ± 746.49	7728.57 ± 774.98	0.835407	0.100	0.404	0.459
GM	Volume of thalamus R	7599.70 ± 737.08	7502.78 ± 770.01	1.073019	0.128	0.284	0.344
DTI	Mean FA in anterior corona radiata L	0.45 ± 0.02	0.48 ± 0.02	-11.1356	-1.337	<0.001	<0.001*
DTI	Mean FA in anterior corona radiata R	0.45 ± 0.02	0.48 ± 0.02	-9.99227	-1.200	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule L	0.58 ± 0.02	0.60 ± 0.02	4977	-0.906	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule R	0.59 ± 0.02	0.61 ± 0.02	5035	-0.885	<0.001	<0.001*
DTI	Mean FA in body of corpus callosum	0.71 ± 0.02	0.74 ± 0.02	3190	-1.341	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle L	0.71 ± 0.02	0.73 ± 0.02	5116	-0.871	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle R	0.70 ± 0.02	0.72 ± 0.02	-7.95269	-0.955	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus L	0.61 ± 0.03	0.64 ± 0.03	-10.104	-1.213	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus R	0.57 ± 0.03	0.60 ± 0.03	4442	-1.064	<0.001	<0.001*

DTI	Mean FA in cingulum hippocampus L	0.45 ± 0.03	0.48 ± 0.03	-6.74618	-0.810	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus R	0.45 ± 0.04	0.47 ± 0.04	6323	-0.633	<0.001	<0.001*
DTI	Mean FA in corticospinal tract L	0.53 ± 0.03	0.55 ± 0.03	-4.36109	-0.524	<0.001	<0.001*
DTI	Mean FA in corticospinal tract R	0.51 ± 0.04	0.53 ± 0.04	-3.73583	-0.449	<0.001	<0.001*
DTI	Mean FA in external capsule L	0.46 ± 0.02	0.48 ± 0.02	-8.93363	-1.073	<0.001	<0.001*
DTI	Mean FA in external capsule R	0.45 ± 0.02	0.47 ± 0.02	-10.1224	-1.215	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis L	0.52 ± 0.03	0.55 ± 0.03	4411	-1.024	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis R	0.52 ± 0.03	0.55 ± 0.03	5013.5	-0.902	<0.001	<0.001*
DTI	Mean FA in fornix	0.45 ± 0.08	0.49 ± 0.06	7003	-0.519	<0.001	<0.001*
DTI	Mean FA in genu of corpus callosum	0.71 ± 0.02	0.75 ± 0.02	2487	-1.535	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle L	0.54 ± 0.03	0.56 ± 0.03	6118.5	-0.634	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle R	0.55 ± 0.02	0.56 ± 0.02	5628	-0.754	<0.001	<0.001*
DTI	Mean FA in medial lemniscus L	0.58 ± 0.03	0.60 ± 0.02	-6.04612	-0.726	<0.001	<0.001*
DTI	Mean FA in medial lemniscus R	0.59 ± 0.02	0.60 ± 0.02	-6.0469	-0.726	<0.001	<0.001*
DTI	Mean FA in middle cerebellar peduncle	0.54 ± 0.02	0.55 ± 0.02	-6.767	-0.812	<0.001	<0.001*
DTI	Mean FA in pontine crossing tract	0.40 ± 0.03	0.42 ± 0.03	7812	-0.330	0.007	0.008*
DTI	Mean FA in posterior corona radiata L	0.47 ± 0.02	0.49 ± 0.02	-10.5438	-1.266	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata R	0.48 ± 0.02	0.51 ± 0.02	-11.3241	-1.360	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule L	0.68 ± 0.02	0.69 ± 0.02	-5.26239	-0.632	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule R	0.67 ± 0.02	0.69 ± 0.02	-6.20392	-0.745	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation L	0.59 ± 0.03	0.62 ± 0.03	3462	-1.240	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation R	0.58 ± 0.03	0.62 ± 0.02	-11.0006	-1.321	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule L	0.61 ± 0.02	0.63 ± 0.02	-6.48208	-0.778	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule R	0.58 ± 0.03	0.60 ± 0.02	-6.63038	-0.796	<0.001	<0.001*
DTI	Mean FA in sagittal stratum L	0.56 ± 0.03	0.58 ± 0.02	-8.90867	-1.070	<0.001	<0.001*
DTI	Mean FA in sagittal stratum R	0.55 ± 0.03	0.58 ± 0.02	-10.3646	-1.244	<0.001	<0.001*
DTI	Mean FA in splenium of corpus callosum	0.78 ± 0.02	0.80 ± 0.02	-9.53981	-1.145	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle L	0.70 ± 0.02	0.71 ± 0.02	6561	-0.571	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle R	0.69 ± 0.02	0.70 ± 0.02	-5.41319	-0.650	<0.001	<0.001*
DTI	Mean FA in superior corona radiata L	0.48 ± 0.02	0.50 ± 0.02	-10.97	-1.317	<0.001	<0.001*
DTI	Mean FA in superior corona radiata R	0.47 ± 0.02	0.50 ± 0.02	-9.5722	-1.149	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus L	0.45 ± 0.03	0.48 ± 0.03	-7.35915	-0.884	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus R	0.45 ± 0.03	0.48 ± 0.04	-5.99567	-0.720	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus L	0.52 ± 0.02	0.54 ± 0.02	-9.05916	-1.088	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus R	0.51 ± 0.02	0.54 ± 0.02	-9.70441	-1.165	<0.001	<0.001*
DTI	Mean FA in tapetum L	0.58 ± 0.06	0.61 ± 0.05	-4.9332	-0.592	<0.001	<0.001*

DTI	Mean FA in tapetum R	0.54 ± 0.06	0.59 ± 0.05	5741	-0.737	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus L	0.50 ± 0.04	0.52 ± 0.03	6670	-0.567	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus R	0.52 ± 0.04	0.54 ± 0.03	6573	-0.599	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	8.257334	0.991	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata R	0.12 ± 0.00	0.12 ± 0.00	7.992028	0.960	<0.001	<0.001*
DTI	Mean AD in anterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	2.607007	0.313	0.010	0.011*
DTI	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	11359.5	0.316	0.010	0.011*
DTI	Mean AD in body of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	12434	0.526	<0.001	<0.001*
DTI	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	0.737159	0.089	0.462	0.462
DTI	Mean AD in cerebral peduncle R	0.14 ± 0.01	0.14 ± 0.01	10585	0.135	0.152	0.161
DTI	Mean AD in cingulum cingulate gyrus L	0.14 ± 0.01	0.14 ± 0.01	1.863628	0.224	0.063	0.072
DTI	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	1.437527	0.173	0.152	0.161
DTI	Mean AD in cingulum hippocampus L	0.12 ± 0.00	0.12 ± 0.00	11520	0.358	0.005	0.006*
DTI	Mean AD in cingulum hippocampus R	0.12 ± 0.01	0.12 ± 0.01	3.38918	0.407	<0.001	0.001*
DTI	Mean AD in corticospinal tract L	0.13 ± 0.01	0.13 ± 0.01	10858.5	0.199	0.066	0.074
DTI	Mean AD in corticospinal tract R	0.13 ± 0.01	0.13 ± 0.01	10694	0.235	0.111	0.121
DTI	Mean AD in external capsule L	0.12 ± 0.00	0.12 ± 0.00	2.278715	0.274	0.023	0.027*
DTI	Mean AD in external capsule R	0.12 ± 0.00	0.12 ± 0.00	3.949206	0.474	<0.001	<0.001*
DTI	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.14 ± 0.01	1.281449	0.154	0.201	0.210
DTI	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	10570	0.171	0.159	0.167
DTI	Mean AD in fornix	0.23 ± 0.02	0.22 ± 0.02	11673.5	0.415	0.002	0.003*
DTI	Mean AD in genu of corpus callosum	0.16 ± 0.01	0.15 ± 0.00	5.56276	0.668	<0.001	<0.001*
DTI	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.00	0.12 ± 0.00	1.60939	0.193	0.109	0.119
DTI	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.00	0.12 ± 0.00	10178	0.071	0.410	0.415
DTI	Mean AD in medial lemniscus L	0.14 ± 0.01	0.13 ± 0.01	10274	0.143	0.333	0.340
DTI	Mean AD in medial lemniscus R	0.14 ± 0.01	0.13 ± 0.01	10728	0.242	0.100	0.112
DTI	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	0.751252	0.090	0.453	0.456
DTI	Mean AD in pontine crossing tract	0.12 ± 0.01	0.11 ± 0.01	10611	0.245	0.141	0.153
DTI	Mean AD in posterior corona radiata L	0.13 ± 0.01	0.12 ± 0.00	15524	1.218	<0.001	<0.001*
DTI	Mean AD in posterior corona radiata R	0.13 ± 0.01	0.13 ± 0.00	15054.5	1.070	<0.001	<0.001*
DTI	Mean AD in posterior limb of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	2.427358	0.291	0.016	0.018*
DTI	Mean AD in posterior limb of internal capsule R	0.14 ± 0.00	0.14 ± 0.00	2.984193	0.358	0.003	0.004*
DTI	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	4.88265	0.586	<0.001	<0.001*
DTI	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.01	12621.5	0.537	<0.001	<0.001*
DTI	Mean AD in retrolenticular part of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	3.881378	0.466	<0.001	<0.001*

DTI	Mean AD in retrolenticular part of internal capsule R	0.14 ± 0.00	0.13 ± 0.00	5.521635	0.663	<0.001	<0.001*
DTI	Mean AD in sagittal stratum L	0.14 ± 0.01	0.13 ± 0.01	12667	0.560	<0.001	<0.001*
DTI	Mean AD in sagittal stratum R	0.14 ± 0.01	0.14 ± 0.01	4.322103	0.519	<0.001	<0.001*
DTI	Mean AD in splenium of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	5.375514	0.645	<0.001	<0.001*
DTI	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	10705.5	0.174	0.107	0.119
DTI	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	10452.5	0.144	0.217	0.225
DTI	Mean AD in superior corona radiata L	0.12 ± 0.00	0.11 ± 0.00	13733.5	0.762	<0.001	<0.001*
DTI	Mean AD in superior corona radiata R	0.12 ± 0.00	0.11 ± 0.00	6.911787	0.830	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.01	0.11 ± 0.01	11978	0.446	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.11 ± 0.01	11688	0.346	0.002	0.003*
DTI	Mean AD in superior longitudinal fasciculus L	0.12 ± 0.00	0.12 ± 0.00	7.800577	0.937	<0.001	<0.001*
DTI	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	7.740829	0.929	<0.001	<0.001*
DTI	Mean AD in tapetum L	0.17 ± 0.02	0.16 ± 0.01	12272.5	0.524	<0.001	<0.001*
DTI	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	12405.5	0.461	<0.001	<0.001*
DTI	Mean AD in uncinate fasciculus L	0.12 ± 0.01	0.12 ± 0.01	1.467211	0.176	0.143	0.154
DTI	Mean AD in uncinate fasciculus R	0.12 ± 0.00	0.12 ± 0.00	10441.5	0.164	0.223	0.230
DTI	Mean RD in anterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	17531.5	1.847	<0.001	<0.001*
DTI	Mean RD in anterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	17341.5	1.764	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	15146.5	0.966	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	14924	0.923	<0.001	<0.001*
DTI	Mean RD in body of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	16807.5	1.543	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle L	0.04 ± 0.00	0.03 ± 0.00	14447.5	0.911	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle R	0.04 ± 0.00	0.03 ± 0.00	14683	0.979	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.04 ± 0.00	13.40323	1.609	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.04 ± 0.00	12.26042	1.472	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.05 ± 0.00	15087.5	1.103	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.05 ± 0.00	14718	0.963	<0.001	<0.001*
DTI	Mean RD in corticospinal tract L	0.05 ± 0.01	0.05 ± 0.01	11858	0.423	<0.001	0.001*
DTI	Mean RD in corticospinal tract R	0.06 ± 0.01	0.05 ± 0.01	11589.5	0.425	0.003	0.004*
DTI	Mean RD in external capsule L	0.05 ± 0.00	0.05 ± 0.00	8.864295	1.064	<0.001	<0.001*
DTI	Mean RD in external capsule R	0.06 ± 0.00	0.05 ± 0.00	15655	1.220	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis L	0.06 ± 0.00	0.05 ± 0.00	14860.5	1.025	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.00	0.05 ± 0.00	14424.5	0.938	<0.001	<0.001*
DTI	Mean RD in fornix	0.11 ± 0.03	0.10 ± 0.02	12015	0.454	<0.001	<0.001*
DTI	Mean RD in genu of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	17292	1.656	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	14231	0.816	<0.001	<0.001*

DTI	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	14307.5	0.877	<0.001	<0.001*
DTI	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	13020	0.614	<0.001	<0.001*
DTI	Mean RD in medial lemniscus R	0.05 ± 0.00	0.05 ± 0.00	13049	0.677	<0.001	<0.001*
DTI	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	13510	0.737	<0.001	<0.001*
DTI	Mean RD in pontine crossing tract	0.06 ± 0.01	0.06 ± 0.01	10916	0.321	0.054	0.062
DTI	Mean RD in posterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	17783	1.831	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	17745.5	1.773	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	6.939747	0.833	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	8.264012	0.992	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.00	16505	1.382	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	16869	1.602	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.00	0.04 ± 0.00	9.034169	1.085	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	15264	1.179	<0.001	<0.001*
DTI	Mean RD in sagittal stratum L	0.05 ± 0.00	0.05 ± 0.00	16291	1.417	<0.001	<0.001*
DTI	Mean RD in sagittal stratum R	0.05 ± 0.00	0.05 ± 0.00	16495	1.451	<0.001	<0.001*
DTI	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.03 ± 0.00	12.37121	1.485	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle L	0.04 ± 0.00	0.04 ± 0.00	5.348065	0.642	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle R	0.04 ± 0.00	0.04 ± 0.00	13148.5	0.690	<0.001	<0.001*
DTI	Mean RD in superior corona radiata L	0.05 ± 0.00	0.05 ± 0.00	17574.5	1.862	<0.001	<0.001*
DTI	Mean RD in superior corona radiata R	0.05 ± 0.00	0.05 ± 0.00	17384	1.825	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.00	0.05 ± 0.00	15114	0.966	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.00	0.05 ± 0.00	14861	0.931	<0.001	<0.001*
DTI	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	13.84549	1.662	<0.001	<0.001*
DTI	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.00	0.05 ± 0.00	17213.5	1.706	<0.001	<0.001*
DTI	Mean RD in tapetum L	0.06 ± 0.01	0.05 ± 0.01	13376.5	0.743	<0.001	<0.001*
DTI	Mean RD in tapetum R	0.07 ± 0.01	0.06 ± 0.01	13823	0.753	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus L	0.05 ± 0.00	0.05 ± 0.00	13297	0.696	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus R	0.05 ± 0.00	0.05 ± 0.00	13562	0.736	<0.001	<0.001*
rs-fMRI	Spos_1	14.46 ± 4.22	11.25 ± 3.05	13898	0.887	<0.001	<0.001*
rs-fMRI	Spos_2	26.20 ± 4.55	24.16 ± 3.71	11894	0.496	<0.001	0.002*
rs-fMRI	Spos_3	17.87 ± 3.87	13.50 ± 3.29	15560	1.227	<0.001	<0.001*
rs-fMRI	Spos_4	25.74 ± 4.01	21.66 ± 4.23	8.164337	0.983	<0.001	<0.001*
rs-fMRI	Spos_5	29.52 ± 3.77	28.33 ± 3.37	2.769493	0.333	0.006	0.013*
rs-fMRI	Spos_6	15.51 ± 3.80	13.02 ± 3.41	13128	0.692	<0.001	<0.001*
rs-fMRI	Spos_7	20.71 ± 4.03	21.98 ± 4.47	-2.44945	-0.295	0.015	0.028*
rs-fMRI	Spos_8	21.40 ± 4.67	16.98 ± 4.08	8.416835	1.013	<0.001	<0.001*
rs-fMRI	Spos_9	20.13 ± 4.14	18.03 ± 3.44	12567	0.558	<0.001	<0.001*

rs-fMRI	Spos_10	24.53 ± 3.99	24.23 ± 3.69	9446	0.080	0.845	0.877
rs-fMRI	Spos_11	30.85 ± 3.89	31.40 ± 3.94	-1.15742	-0.139	0.248	0.317
rs-fMRI	Spos_12	27.44 ± 3.27	26.87 ± 3.27	1.43695	0.173	0.152	0.223
rs-fMRI	Spos_13	22.33 ± 3.81	22.93 ± 3.83	-1.30091	-0.157	0.194	0.271
rs-fMRI	Spos_14	21.87 ± 3.72	17.15 ± 3.28	11.23016	1.352	<0.001	<0.001*
rs-fMRI	Spos_15	20.78 ± 4.21	19.47 ± 3.84	2.701272	0.325	0.007	0.015*
rs-fMRI	Spos_16	14.72 ± 4.07	9.80 ± 3.77	15713	1.256	<0.001	<0.001*
rs-fMRI	Spos_17	14.32 ± 3.68	13.23 ± 3.44	2.568439	0.309	0.011	0.021*
rs-fMRI	Spos_18	24.64 ± 4.47	22.67 ± 3.47	12158	0.498	<0.001	<0.001*
rs-fMRI	Spos_19	23.29 ± 3.53	21.83 ± 3.66	3.340925	0.402	<0.001	0.002*
rs-fMRI	Spos_20	14.79 ± 3.28	12.37 ± 3.42	13469	0.718	<0.001	<0.001*
rs-fMRI	Spos_21	22.54 ± 3.85	23.07 ± 3.47	-1.21165	-0.146	0.227	0.304
rs-fMRI	Spos_22	19.16 ± 4.37	17.42 ± 3.72	11973	0.434	<0.001	0.001*
rs-fMRI	Spos_23	13.22 ± 3.33	10.42 ± 3.15	14259	0.865	<0.001	<0.001*
rs-fMRI	Spos_24	33.00 ± 3.72	31.03 ± 3.90	4.274883	0.515	<0.001	<0.001*
rs-fMRI	Spos_25	25.34 ± 4.19	23.59 ± 4.10	3.498964	0.421	<0.001	0.002*
rs-fMRI	Spos_26	24.19 ± 3.67	22.12 ± 3.24	4.994194	0.601	<0.001	<0.001*
rs-fMRI	Spos_27	19.98 ± 4.12	17.79 ± 4.31	12667	0.519	<0.001	<0.001*
rs-fMRI	Spos_28	20.57 ± 3.95	19.68 ± 3.78	1.909769	0.230	0.057	0.101
rs-fMRI	Spos_29	28.33 ± 4.28	27.00 ± 4.19	2.614397	0.315	0.009	0.019*
rs-fMRI	Spos_30	14.04 ± 3.44	10.97 ± 2.63	14787	1.017	<0.001	<0.001*
rs-fMRI	Spos_31	28.03 ± 4.21	28.11 ± 4.44	-0.16585	-0.020	0.868	0.888
rs-fMRI	Spos_32	15.71 ± 3.41	12.82 ± 3.24	14245	0.871	<0.001	<0.001*
rs-fMRI	Spos_33	21.81 ± 3.52	21.27 ± 3.92	1.212091	0.146	0.227	0.304
rs-fMRI	Spos_34	19.02 ± 3.18	17.63 ± 2.99	3.750833	0.451	<0.001	<0.001*
rs-fMRI	Spos_35	18.47 ± 4.02	16.85 ± 3.68	11760	0.420	0.001	0.003*
rs-fMRI	Spos_36	24.09 ± 3.90	23.29 ± 3.41	1.809776	0.218	0.071	0.119
rs-fMRI	Spos_37	27.40 ± 3.95	27.17 ± 4.01	9650	0.058	0.914	0.922
rs-fMRI	Spos_38	13.70 ± 3.65	11.21 ± 2.94	13527	0.759	<0.001	<0.001*
rs-fMRI	Spos_39	31.55 ± 3.28	30.93 ± 3.66	1.463057	0.176	0.145	0.218
rs-fMRI	Spos_40	18.55 ± 3.74	18.70 ± 4.32	9296	-0.036	0.675	0.742
rs-fMRI	Spos_41	22.20 ± 4.75	17.26 ± 3.62	15246	1.187	<0.001	<0.001*
rs-fMRI	Spos_42	20.98 ± 3.55	17.61 ± 3.08	8.491266	1.022	<0.001	<0.001*
rs-fMRI	Spos_43	9.70 ± 2.90	9.49 ± 2.72	10276	0.076	0.296	0.370
rs-fMRI	Spos_44	22.72 ± 3.97	23.67 ± 4.31	-1.89705	-0.228	0.059	0.103
rs-fMRI	Spos_45	20.26 ± 3.80	21.50 ± 4.35	8023	-0.300	0.020	0.038*
rs-fMRI	Spos_46	17.13 ± 4.44	17.08 ± 4.06	9420	0.012	0.815	0.862
rs-fMRI	Spos_47	21.87 ± 4.27	21.77 ± 4.44	0.195933	0.024	0.845	0.877
rs-fMRI	Spos_48	22.57 ± 3.88	21.76 ± 3.15	10476	0.232	0.179	0.256
rs-fMRI	Spos_49	31.16 ± 4.33	29.00 ± 4.26	4.169172	0.502	<0.001	<0.001*
rs-fMRI	Spos_50	11.58 ± 2.92	12.07 ± 3.15	8758	-0.160	0.221	0.304
rs-fMRI	Spos_51	12.40 ± 3.04	11.48 ± 2.73	11214	0.321	0.014	0.028*
rs-fMRI	Spos_52	12.84 ± 3.20	11.67 ± 2.81	11725	0.391	0.001	0.003*
rs-fMRI	Spos_53	13.45 ± 3.62	14.09 ± 3.87	8692	-0.170	0.186	0.262

rs-fMRI	Spos_54	11.82 ± 2.83	11.29 ± 2.74	1.589631	0.191	0.113	0.173
rs-fMRI	Spos_55	9.83 ± 2.30	9.64 ± 2.22	10069	0.081	0.462	0.547
rs-fMRI	Sneg_1	21.70 ± 5.31	14.59 ± 4.95	16152	1.389	<0.001	<0.001*
rs-fMRI	Sneg_2	28.32 ± 4.37	28.36 ± 4.23	-0.0678	-0.008	0.946	0.946
rs-fMRI	Sneg_3	21.57 ± 4.11	17.06 ± 4.07	9.152114	1.102	<0.001	<0.001*
rs-fMRI	Sneg_4	29.78 ± 5.69	24.50 ± 5.96	7.489253	0.901	<0.001	<0.001*
rs-fMRI	Sneg_5	28.35 ± 4.51	28.99 ± 4.38	8331	-0.142	0.062	0.107
rs-fMRI	Sneg_6	22.70 ± 6.79	18.67 ± 7.74	12795	0.548	<0.001	<0.001*
rs-fMRI	Sneg_7	22.67 ± 4.48	23.17 ± 4.65	9105	-0.109	0.481	0.562
rs-fMRI	Sneg_8	22.74 ± 6.66	16.25 ± 4.93	14967	1.125	<0.001	<0.001*
rs-fMRI	Sneg_9	20.34 ± 4.67	19.36 ± 3.71	10647	0.235	0.110	0.171
rs-fMRI	Sneg_10	24.99 ± 5.03	25.58 ± 5.14	-0.96168	-0.116	0.337	0.413
rs-fMRI	Sneg_11	26.67 ± 4.32	28.19 ± 3.64	7597	-0.382	0.003	0.007*
rs-fMRI	Sneg_12	28.92 ± 4.96	31.84 ± 4.94	-4.88431	-0.588	<0.001	<0.001*
rs-fMRI	Sneg_13	22.35 ± 4.18	22.84 ± 4.32	-0.96034	-0.116	0.338	0.413
rs-fMRI	Sneg_14	26.32 ± 5.72	22.29 ± 5.16	6.16885	0.743	<0.001	<0.001*
rs-fMRI	Sneg_15	23.18 ± 4.51	22.32 ± 4.20	10535	0.196	0.152	0.223
rs-fMRI	Sneg_16	17.92 ± 6.74	11.38 ± 5.49	14978	1.075	<0.001	<0.001*
rs-fMRI	Sneg_17	19.03 ± 3.57	18.65 ± 3.21	0.942133	0.113	0.347	0.415
rs-fMRI	Sneg_18	26.89 ± 4.85	26.17 ± 5.13	1.186795	0.143	0.236	0.309
rs-fMRI	Sneg_19	24.31 ± 5.00	23.48 ± 4.98	1.366556	0.164	0.173	0.250
rs-fMRI	Sneg_20	20.65 ± 5.58	16.28 ± 4.91	13814	0.836	<0.001	<0.001*
rs-fMRI	Sneg_21	20.98 ± 4.04	21.75 ± 4.03	-1.60026	-0.193	0.111	0.171
rs-fMRI	Sneg_22	18.13 ± 4.87	17.66 ± 4.06	10001	0.107	0.526	0.603
rs-fMRI	Sneg_23	17.49 ± 3.64	15.94 ± 3.30	12006	0.448	<0.001	<0.001*
rs-fMRI	Sneg_24	28.02 ± 3.88	28.20 ± 4.57	-0.34682	-0.042	0.729	0.786
rs-fMRI	Sneg_25	22.97 ± 4.46	21.78 ± 4.42	2.222596	0.268	0.027	0.050
rs-fMRI	Sneg_26	25.76 ± 4.30	25.37 ± 4.73	10209	0.086	0.345	0.415
rs-fMRI	Sneg_27	22.83 ± 3.61	20.65 ± 3.97	12452	0.570	<0.001	<0.001*
rs-fMRI	Sneg_28	21.25 ± 5.45	23.08 ± 5.73	-2.69147	-0.324	0.008	0.015*
rs-fMRI	Sneg_29	23.53 ± 4.86	22.85 ± 4.86	1.173098	0.141	0.242	0.313
rs-fMRI	Sneg_30	18.70 ± 5.74	15.13 ± 4.93	13365	0.673	<0.001	<0.001*
rs-fMRI	Sneg_31	23.88 ± 4.39	24.89 ± 4.14	8216	-0.236	0.042	0.075
rs-fMRI	Sneg_32	19.31 ± 6.29	14.84 ± 5.05	13661	0.792	<0.001	<0.001*
rs-fMRI	Sneg_33	21.35 ± 4.34	23.10 ± 4.79	-3.14695	-0.379	0.002	0.004*
rs-fMRI	Sneg_34	25.76 ± 4.73	24.29 ± 4.68	11594	0.311	0.003	0.006*
rs-fMRI	Sneg_35	19.06 ± 4.18	17.58 ± 3.45	11398	0.390	0.006	0.014*
rs-fMRI	Sneg_36	25.47 ± 3.95	24.67 ± 4.54	10796	0.187	0.068	0.116
rs-fMRI	Sneg_37	25.50 ± 4.45	25.28 ± 4.44	0.424221	0.051	0.672	0.742
rs-fMRI	Sneg_38	13.67 ± 3.39	12.36 ± 2.94	11796	0.416	<0.001	0.002*
rs-fMRI	Sneg_39	28.15 ± 5.31	27.12 ± 4.67	1.725416	0.208	0.086	0.140
rs-fMRI	Sneg_40	22.33 ± 3.55	22.07 ± 3.91	9794	0.069	0.746	0.797
rs-fMRI	Sneg_41	22.33 ± 5.93	17.16 ± 4.25	14709	1.021	<0.001	<0.001*
rs-fMRI	Sneg_42	22.76 ± 4.14	20.57 ± 4.31	4.283699	0.516	<0.001	<0.001*

rs-fMRI	Sneg_43	17.37 ± 4.00	16.06 ± 3.72	11593	0.342	0.003	0.006*
rs-fMRI	Sneg_44	21.48 ± 4.19	22.25 ± 3.51	-1.67411	-0.202	0.095	0.154
rs-fMRI	Sneg_45	18.05 ± 4.01	18.77 ± 3.88	8472	-0.183	0.099	0.157
rs-fMRI	Sneg_46	18.47 ± 3.50	18.64 ± 3.33	-0.3971	-0.048	0.692	0.753
rs-fMRI	Sneg_47	17.21 ± 4.34	17.06 ± 4.42	9868	0.036	0.664	0.742
rs-fMRI	Sneg_48	20.32 ± 3.87	20.93 ± 4.45	-1.20319	-0.145	0.230	0.305
rs-fMRI	Sneg_49	19.53 ± 3.91	19.28 ± 3.90	0.526702	0.063	0.599	0.679
rs-fMRI	Sneg_50	15.94 ± 3.38	15.91 ± 3.41	9685	0.009	0.872	0.888
rs-fMRI	Sneg_51	18.42 ± 3.99	16.91 ± 3.27	11869	0.416	<0.001	0.002*
rs-fMRI	Sneg_52	17.46 ± 3.57	16.17 ± 3.27	3.152601	0.379	0.002	0.004*
rs-fMRI	Sneg_53	13.69 ± 3.64	14.39 ± 4.25	8829	-0.176	0.264	0.333
rs-fMRI	Sneg_54	16.17 ± 4.51	14.74 ± 3.33	11458	0.366	0.005	0.011*
rs-fMRI	Sneg_55	10.91 ± 2.19	11.15 ± 2.22	9150	-0.107	0.523	0.603
t-fMRI	Median z-statistic (amygdala) for faces-shapes contrast	0.67 ± 0.80	1.52 ± 0.80	-8.24033	-1.052	<0.001	<0.001*
t-fMRI	Median z-statistic for faces activation	1.55 ± 1.03	3.37 ± 0.94	1451.5	-1.878	<0.001	<0.001*
t-fMRI	Median z-statistic for shapes activation	1.59 ± 1.15	3.07 ± 1.08	-10.5103	-1.342	<0.001	<0.001*
t-fMRI	Median z-statistic for faces-shapes contrast	1.50 ± 1.16	3.10 ± 1.19	-10.6339	-1.358	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic (amygdala) for faces-shapes contrast	2.27 ± 0.91	3.33 ± 0.97	3707	-1.112	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces activation	4.47 ± 1.45	7.06 ± 1.29	1295	-1.924	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for shapes activation	4.25 ± 1.58	6.32 ± 1.43	-10.8967	-1.392	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces-shapes contrast	4.43 ± 1.61	6.97 ± 1.68	2019	-1.527	<0.001	<0.001*
t-fMRI	Left amygdala habituation for faces condition	-0.16 ± 0.33	0.15 ± 0.23	3429	-1.185	<0.001	<0.001*
t-fMRI	Right amygdala habituation for faces condition	-0.15 ± 0.31	0.14 ± 0.20	3265	-1.200	<0.001	<0.001*
t-fMRI	Left amygdala habituation for shapes condition	-0.11 ± 0.40	0.11 ± 0.22	5276	-0.762	<0.001	<0.001*
t-fMRI	Right amygdala habituation for shapes condition	-0.07 ± 0.33	0.11 ± 0.22	5316	-0.694	<0.001	<0.001*
PGSs	ADHD Demontis2022	0.41 ± 0.56	0.33 ± 0.58	10847	0.133	0.075	0.145
PGSs	ALCDEP Walters2018	-1.13 ± 0.22	-1.11 ± 0.24	9427	-0.085	0.738	0.843
PGSs	AN Watson2019	-4.31 ± 0.61	-4.26 ± 0.75	9350	-0.072	0.653	0.800
PGSs	ASD Grove2019	-0.30 ± 0.35	-0.35 ± 0.40	1.057502	0.127	0.291	0.432
PGSs	BD PGC4 2025	-1.37 ± 0.54	-1.43 ± 0.58	0.862246	0.103	0.389	0.531
PGSs	BMI Locke2015	0.37 ± 0.21	0.30 ± 0.22	2.530661	0.303	0.012	0.028*
PGSs	bNGF Konieczny2025	0.00 ± 0.04	-0.02 ± 0.03	5.134803	0.616	<0.001	<0.001*
PGSs	CAD Nikpay2015	0.94 ± 0.43	0.92 ± 0.43	0.396244	0.048	0.692	0.829
PGSs	CCL11 Konieczny2025	-0.76 ± 0.25	-0.81 ± 0.23	10806	0.201	0.086	0.161
PGSs	CCL2 Konieczny2025	0.26 ± 0.55	0.27 ± 0.54	9433	-0.016	0.745	0.843
PGSs	CCL3 Konieczny2025	-0.43 ± 0.32	-0.45 ± 0.32	0.579353	0.069	0.563	0.734
PGSs	CCL4 Konieczny2025	0.56 ± 0.35	0.54 ± 0.44	9834	0.045	0.787	0.874
PGSs	CCL7 Konieczny2025	-0.88 ± 0.34	-0.97 ± 0.38	11013	0.247	0.043	0.091
PGSs	CRP Said2022	0.39 ± 0.40	0.29 ± 0.38	10966	0.246	0.050	0.104
PGSs	CSF1 Konieczny2025	0.62 ± 0.65	0.73 ± 0.64	8693	-0.174	0.153	0.263
PGSs	CSF3 Konieczny2025	0.47 ± 0.30	0.47 ± 0.31	9612	0.004	0.953	0.975

PGSs	CTACK Konieczny2025	-0.02 ± 0.05	-0.06 ± 0.04	14815	0.990	<0.001	<0.001*
PGSs	CUD Johnson2020	-1.13 ± 0.34	-1.13 ± 0.37	10028	0.010	0.576	0.735
PGSs	CXCL1 Konieczny2025	-3.38 ± 0.80	-3.43 ± 0.80	10130	0.063	0.477	0.636
PGSs	CXCL10 Konieczny2025	-0.06 ± 0.09	-0.12 ± 0.10	12952	0.568	<0.001	<0.001*
PGSs	CXCL12 Konieczny2025	0.18 ± 0.13	0.16 ± 0.14	1.310187	0.157	0.191	0.310
PGSs	CXCL9 Konieczny2025	0.01 ± 0.08	-0.04 ± 0.08	5.255462	0.630	<0.001	<0.001*
PGSs	FGFb Konieczny2025	0.59 ± 0.35	0.52 ± 0.38	1.519908	0.182	0.130	0.229
PGSs	GAD FinnGen2024	0.11 ± 0.29	0.15 ± 0.26	-1.12832	-0.135	0.260	0.400
PGSs	HbA1c Willems2023	0.11 ± 0.07	0.13 ± 0.07	-2.76558	-0.332	0.006	0.015*
PGSs	HDL Graham2021	1.79 ± 0.44	1.94 ± 0.43	-2.76828	-0.332	0.006	0.015*
PGSs	HGF Konieczny2025	0.41 ± 0.13	0.32 ± 0.12	5.484559	0.658	<0.001	<0.001*
PGSs	IFNg Konieczny2025	0.17 ± 0.08	0.04 ± 0.08	16564	1.530	<0.001	<0.001*
PGSs	IL10 Konieczny2025	0.07 ± 0.04	0.02 ± 0.04	11.27063	1.351	<0.001	<0.001*
PGSs	IL13 Konieczny2025	0.05 ± 0.07	-0.07 ± 0.07	14.3408	1.719	<0.001	<0.001*
PGSs	IL16 Konieczny2025	0.34 ± 0.46	0.29 ± 0.46	10279	0.121	0.351	0.489
PGSs	IL17 Konieczny2025	0.09 ± 0.03	0.03 ± 0.03	14.9301	1.790	<0.001	<0.001*
PGSs	IL18 Konieczny2025	1.26 ± 1.13	1.26 ± 1.11	9655	0.002	0.997	0.997
PGSs	IL1b Konieczny2025	-0.77 ± 0.19	-0.77 ± 0.16	0.197017	0.024	0.844	0.921
PGSs	IL1RA Konieczny2025	-0.25 ± 0.19	-0.32 ± 0.15	11805	0.426	0.001	0.004*
PGSs	IL2 Konieczny2025	0.20 ± 0.07	0.15 ± 0.07	6.014424	0.721	<0.001	<0.001*
PGSs	IL2RA Konieczny2025	0.09 ± 0.06	0.08 ± 0.07	10486	0.146	0.214	0.338
PGSs	IL4 Konieczny2025	0.09 ± 0.03	0.03 ± 0.04	17013	1.649	<0.001	<0.001*
PGSs	IL5 Konieczny2025	0.12 ± 0.04	0.06 ± 0.03	16622	1.530	<0.001	<0.001*
PGSs	IL6 Konieczny2025	0.10 ± 0.06	0.07 ± 0.06	5.701936	0.684	<0.001	<0.001*
PGSs	IL7 Konieczny2025	0.01 ± 0.03	-0.05 ± 0.03	17.9015	2.146	<0.001	<0.001*
PGSs	IL8 Konieczny2025	0.19 ± 0.08	0.10 ± 0.09	9.067447	1.087	<0.001	<0.001*
PGSs	IL9 Konieczny2025	0.16 ± 0.07	0.08 ± 0.08	8.759834	1.050	<0.001	<0.001*
PGSs	LDL Graham2021	0.31 ± 0.44	0.28 ± 0.43	0.541234	0.065	0.589	0.736
PGSs	MDD PGC4 2025	-0.79 ± 0.34	-0.84 ± 0.41	10355	0.124	0.295	0.432
PGSs	MIF Konieczny2025	0.04 ± 0.04	0.03 ± 0.04	2.874891	0.345	0.004	0.011*
PGSs	NEUROT DeMoor2015	-0.15 ± 0.05	-0.15 ± 0.05	0.059624	0.007	0.952	0.975
PGSs	OCD PGC3 2018	-0.06 ± 0.32	-0.05 ± 0.33	-0.3789	-0.045	0.705	0.829
PGSs	PDGFbB Konieczny2025	0.23 ± 0.15	0.14 ± 0.16	4.778362	0.573	<0.001	<0.001*
PGSs	PTSD Nievergelt2024	-0.29 ± 0.30	-0.36 ± 0.30	1.879216	0.225	0.061	0.123
PGSs	RANTES Konieczny2025	0.22 ± 0.17	0.15 ± 0.16	3.513047	0.421	<0.001	0.002*
PGSs	SCF Konieczny2025	0.82 ± 0.23	0.85 ± 0.24	9012	-0.140	0.341	0.487
PGSs	SCGFb Konieczny2025	-0.00 ± 0.28	-0.06 ± 0.23	10542	0.219	0.185	0.308
PGSs	SCZ Trubetskoy2022	-4.90 ± 1.07	-5.10 ± 1.21	11310	0.181	0.014	0.030*
PGSs	T2D Verma2024	-12.29 ± 0.99	-12.39 ± 1.34	10796	0.082	0.088	0.161
PGSs	TNFa Konieczny2025	0.10 ± 0.03	0.04 ± 0.03	17583	1.819	<0.001	<0.001*
PGSs	TNFb Konieczny2025	0.09 ± 0.04	0.02 ± 0.04	15.74394	1.888	<0.001	<0.001*
PGSs	TRAIL Konieczny2025	-0.24 ± 0.41	-0.27 ± 0.36	9710	0.087	0.932	0.975
PGSs	TRIG Graham2021	-1.36 ± 0.36	-1.51 ± 0.39	11892	0.394	<0.001	0.002*
PGSs	VEGF Konieczny2025	-0.58 ± 0.30	-0.57 ± 0.32	-0.05164	-0.006	0.959	0.975

Multimodal	Area of caudalanteriorcingulate L	1060.33 ± 183.21	1048.85 ± 173.15	9741	0.064	0.934	0.962
Multimodal	Area of caudalanteriorcingulate R	763.83 ± 178.91	745.01 ± 142.20	10038.5	0.117	0.600	0.733
Multimodal	Area of caudalmiddlefrontal L	2357.54 ± 390.69	2315.62 ± 313.26	9982.5	0.119	0.659	0.775
Multimodal	Area of caudalmiddlefrontal R	2174.98 ± 368.62	2164.19 ± 335.67	9725.5	0.031	0.953	0.969
Multimodal	Area of cuneus L	2040.74 ± 283.61	2090.91 ± 282.82	8798	-0.177	0.187	0.312
Multimodal	Area of cuneus R	1955.79 ± 253.76	1996.81 ± 264.33	8717	-0.158	0.150	0.264
Multimodal	Area of entorhinal L	407.88 ± 77.52	409.88 ± 74.09	9406	-0.026	0.679	0.790
Multimodal	Area of entorhinal R	373.88 ± 68.98	361.25 ± 67.13	10755.5	0.185	0.111	0.204
Multimodal	Area of fusiform L	2797.72 ± 364.55	2763.03 ± 317.61	9967.5	0.102	0.675	0.787
Multimodal	Area of fusiform R	2749.30 ± 370.35	2744.66 ± 343.39	9500.5	0.013	0.784	0.882
Multimodal	Area of inferiorparietal L	4271.50 ± 600.56	4196.13 ± 542.45	10613	0.132	0.168	0.284
Multimodal	Area of inferiorparietal R	4990.58 ± 692.79	4915.32 ± 646.74	10282	0.112	0.375	0.516
Multimodal	Area of inferiortemporal L	3336.26 ± 413.98	3354.42 ± 439.55	9696.5	-0.042	0.987	0.987
Multimodal	Area of inferiortemporal R	3572.97 ± 475.69	3493.28 ± 434.03	10532.5	0.175	0.208	0.339
Multimodal	Area of insula L	1959.96 ± 201.02	1929.70 ± 190.02	10527.5	0.155	0.210	0.341
Multimodal	Area of insula R	2058.21 ± 210.14	2021.50 ± 195.31	10601	0.181	0.173	0.292
Multimodal	Area of isthmuscingulate L	997.90 ± 172.57	997.46 ± 145.37	9623	0.003	0.927	0.958
Multimodal	Area of isthmuscingulate R	873.72 ± 138.90	890.09 ± 143.50	9162	-0.115	0.437	0.575
Multimodal	Area of lateraloccipital L	4971.75 ± 652.71	5004.01 ± 553.97	9254	-0.053	0.522	0.666
Multimodal	Area of lateraloccipital R	4986.26 ± 658.15	5072.38 ± 653.46	8921.5	-0.131	0.256	0.391
Multimodal	Area of lateralorbitofrontal L	2933.52 ± 316.45	2881.91 ± 285.42	1.43215	0.171	0.153	0.265
Multimodal	Area of lateralorbitofrontal R	2936.94 ± 353.58	2909.83 ± 301.51	0.691301	0.083	0.490	0.632
Multimodal	Area of lingual L	3078.02 ± 390.00	3157.96 ± 394.03	-1.69844	-0.203	0.091	0.173
Multimodal	Area of lingual R	3162.02 ± 415.33	3206.61 ± 422.23	8778	-0.106	0.178	0.297
Multimodal	Area of medialorbitofrontal L	1575.85 ± 179.21	1552.05 ± 165.96	1.150877	0.138	0.251	0.386
Multimodal	Area of medialorbitofrontal R	1492.69 ± 181.09	1480.17 ± 162.18	10091.5	0.073	0.546	0.689
Multimodal	Area of middletemporal L	4133.15 ± 563.37	4061.09 ± 489.88	10303	0.137	0.358	0.500
Multimodal	Area of middletemporal R	4103.54 ± 523.31	4049.49 ± 438.23	9996	0.112	0.644	0.763
Multimodal	Area of paracentral L	1579.03 ± 216.78	1560.72 ± 186.80	10052	0.091	0.586	0.721
Multimodal	Area of paracentral R	1566.22 ± 213.88	1546.81 ± 183.20	10084	0.098	0.553	0.695
Multimodal	Area of parahippocampal L	689.12 ± 80.64	686.09 ± 74.34	9858.5	0.039	0.797	0.889
Multimodal	Area of parahippocampal R	669.35 ± 71.43	668.29 ± 71.25	0.124425	0.015	0.901	0.944
Multimodal	Area of parsopercularis L	1455.27 ± 225.37	1381.15 ± 186.65	11675	0.360	0.003	0.009*
Multimodal	Area of parsopercularis R	1555.26 ± 247.67	1506.17 ± 206.23	10753.5	0.216	0.112	0.204
Multimodal	Area of parsorbitalis L	673.67 ± 85.98	656.45 ± 77.57	10649.5	0.210	0.152	0.265

Multimodal	Area of parsorbitalis R	701.11 ± 106.88	678.60 ± 96.09	11054	0.222	0.042	0.092
Multimodal	Area of parstriangularis L	1581.08 ± 250.28	1507.50 ± 221.81	11245.5	0.312	0.020	0.049*
Multimodal	Area of parstriangularis R	1461.26 ± 233.30	1430.05 ± 209.99	10477.5	0.141	0.239	0.373
Multimodal	Area of pericalcarine L	1342.45 ± 250.29	1427.85 ± 244.45	7812.5	-0.345	0.005	0.014*
Multimodal	Area of pericalcarine R	1485.67 ± 270.53	1554.95 ± 265.38	-2.15554	-0.258	0.032	0.074
Multimodal	Area of postcentral L	4556.33 ± 524.31	4555.48 ± 445.92	9546	0.002	0.837	0.909
Multimodal	Area of postcentral R	4363.82 ± 595.12	4272.60 ± 461.20	10270	0.172	0.385	0.525
Multimodal	Area of posteriorcingulate L	1236.88 ± 184.69	1235.72 ± 178.31	9632.5	0.006	0.938	0.962
Multimodal	Area of posteriorcingulate R	1193.35 ± 174.02	1182.77 ± 154.42	9852.5	0.064	0.804	0.889
Multimodal	Area of precentral L	4606.68 ± 498.35	4617.59 ± 497.74	9586.5	-0.022	0.884	0.937
Multimodal	Area of precentral R	4456.90 ± 526.76	4475.13 ± 523.27	9632	-0.035	0.938	0.962
Multimodal	Area of precuneus L	3671.72 ± 483.68	3568.70 ± 407.26	10586	0.231	0.180	0.301
Multimodal	Area of precuneus R	4001.94 ± 551.53	3937.85 ± 516.17	10314.5	0.120	0.349	0.489
Multimodal	Area of rostralanteriorcingulate L	1156.88 ± 215.45	1148.09 ± 193.67	9550	0.043	0.841	0.911
Multimodal	Area of rostralanteriorcingulate R	805.53 ± 179.74	782.38 ± 136.92	10202	0.146	0.442	0.580
Multimodal	Area of rostralmiddlefrontal L	3882.30 ± 566.71	3907.05 ± 546.57	9423.5	-0.044	0.698	0.807
Multimodal	Area of rostralmiddlefrontal R	4026.10 ± 573.78	4041.68 ± 571.34	9439.5	-0.027	0.716	0.822
Multimodal	Area of superiorfrontal L	7651.91 ± 966.21	7581.15 ± 854.76	9788	0.078	0.879	0.935
Multimodal	Area of superiorfrontal R	8691.54 ± 1042.25	8705.22 ± 978.19	9390	-0.014	0.661	0.776
Multimodal	Area of superiorparietal L	4299.69 ± 575.20	4171.01 ± 536.81	10953	0.231	0.059	0.125
Multimodal	Area of superiorparietal R	4372.64 ± 612.57	4283.36 ± 551.40	10123.5	0.153	0.515	0.659
Multimodal	Area of superiortemporal L	4998.82 ± 604.53	4982.33 ± 496.05	9581.5	0.030	0.878	0.935
Multimodal	Area of superiortemporal R	4687.31 ± 535.39	4680.12 ± 429.90	9538	0.015	0.827	0.907
Multimodal	Area of supramarginal L	3571.08 ± 620.89	3519.51 ± 509.94	10098.5	0.091	0.539	0.682
Multimodal	Area of supramarginal R	3405.68 ± 513.30	3351.04 ± 418.09	10222.5	0.117	0.424	0.565
Multimodal	Area of transversetemporal L	453.29 ± 82.71	448.66 ± 68.50	9721	0.061	0.958	0.971
Multimodal	Area of transversetemporal R	332.99 ± 54.93	326.42 ± 45.04	10362.5	0.131	0.314	0.456
Multimodal	Volume of caudalanteriorcingulate L	3049.98 ± 606.88	3105.77 ± 581.20	8864.5	-0.094	0.223	0.355
Multimodal	Volume of caudalanteriorcingulate R	2229.31 ± 527.90	2209.45 ± 530.57	9617	0.037	0.920	0.955
Multimodal	Volume of caudalmiddlefrontal L	7022.42 ± 1196.26	7278.50 ± 1027.60	7972.5	-0.230	0.011	0.028*
Multimodal	Volume of caudalmiddlefrontal R	6489.87 ± 1162.96	6733.75 ± 1067.82	8288	-0.218	0.038	0.084
Multimodal	Volume of cuneus L	4131.89 ± 624.08	4547.53 ± 753.83	6714	-0.595	<0.001	<0.001*
Multimodal	Volume of cuneus R	3716.48 ± 529.16	4057.23 ± 643.44	6590	-0.573	<0.001	<0.001*
Multimodal	Volume of entorhinal L	1673.21 ± 341.03	1784.44 ± 331.19	7485.5	-0.330	0.001	0.003*
Multimodal	Volume of entorhinal R	1627.47 ± 310.18	1665.87 ± 267.57	8708	-0.133	0.146	0.258

Multimodal	Volume of fusiform L	8860.90 ± 1235.10	9137.59 ± 1130.89	8173	-0.234	0.025	0.058
Multimodal	Volume of fusiform R	8758.62 ± 1228.96	9097.21 ± 1160.37	7869	-0.283	0.007	0.018*
Multimodal	Volume of inferiorparietal L	12231.97 ± 1800.63	12528.45 ± 1708.18	-1.41015	-0.169	0.160	0.273
Multimodal	Volume of inferiorparietal R	14569.24 ± 2005.33	14953.32 ± 2013.01	8775.5	-0.191	0.176	0.296
Multimodal	Volume of inferiortemporal L	12179.21 ± 1649.87	12688.90 ± 1650.15	7980.5	-0.308	0.011	0.028*
Multimodal	Volume of inferiortemporal R	12482.44 ± 1779.60	12769.99 ± 1629.20	8510	-0.169	0.081	0.157
Multimodal	Volume of insula L	6166.58 ± 688.82	6285.38 ± 606.95	8485	-0.183	0.074	0.150
Multimodal	Volume of insula R	6446.98 ± 726.12	6540.72 ± 663.86	8739	-0.135	0.160	0.273
Multimodal	Volume of isthmuscingulate L	2678.32 ± 449.16	2711.89 ± 381.70	9056	-0.081	0.350	0.489
Multimodal	Volume of isthmuscingulate R	2481.81 ± 385.93	2601.41 ± 424.20	8279.5	-0.293	0.037	0.082
Multimodal	Volume of lateraloccipital L	12167.47 ± 1739.87	12886.95 ± 1562.79	7239	-0.435	<0.001	<0.001*
Multimodal	Volume of lateraloccipital R	12327.57 ± 1694.97	13134.44 ± 1824.04	7113	-0.456	<0.001	<0.001*
Multimodal	Volume of lateralorbitofrontal L	8914.64 ± 1023.30	9153.54 ± 932.42	-2.03994	-0.244	0.042	0.092
Multimodal	Volume of lateralorbitofrontal R	8971.12 ± 978.75	9205.37 ± 920.72	8196.5	-0.246	0.027	0.063
Multimodal	Volume of lingual L	6291.56 ± 1028.68	6856.68 ± 1126.79	-4.35102	-0.521	<0.001	<0.001*
Multimodal	Volume of lingual R	6416.55 ± 926.24	6710.96 ± 1105.65	7931	-0.286	0.009	0.023*
Multimodal	Volume of medialorbitofrontal L	4928.58 ± 616.59	4997.19 ± 580.49	-0.95657	-0.114	0.340	0.479
Multimodal	Volume of medialorbitofrontal R	4817.92 ± 524.75	4849.49 ± 537.84	-0.49472	-0.059	0.621	0.748
Multimodal	Volume of middletemporal L	13879.38 ± 2026.87	14171.40 ± 1820.69	8642	-0.152	0.121	0.219
Multimodal	Volume of middletemporal R	13920.28 ± 1849.80	14401.44 ± 1655.40	7815.5	-0.274	0.005	0.014*
Multimodal	Volume of paracentral L	4450.31 ± 615.02	4695.06 ± 552.06	7200.5	-0.419	<0.001	<0.001*
Multimodal	Volume of paracentral R	4335.98 ± 597.83	4540.54 ± 544.46	7724.5	-0.358	0.004	0.010*
Multimodal	Volume of parahippocampal L	2090.70 ± 292.62	2223.36 ± 296.55	6836	-0.449	<0.001	<0.001*
Multimodal	Volume of parahippocampal R	1990.55 ± 235.36	2073.70 ± 235.26	7794.5	-0.352	0.005	0.013*
Multimodal	Volume of parsopercularis L	4534.12 ± 755.20	4517.46 ± 693.49	9748.5	0.023	0.925	0.958
Multimodal	Volume of parsopercularis R	4704.94 ± 767.40	4727.34 ± 700.53	9420	-0.030	0.694	0.806
Multimodal	Volume of parsorbitalis L	2202.93 ± 313.29	2256.99 ± 303.67	8522.5	-0.175	0.084	0.163
Multimodal	Volume of parsorbitalis R	2308.64 ± 356.30	2325.97 ± 321.40	9562	-0.051	0.855	0.922
Multimodal	Volume of parstriangularis L	4570.76 ± 742.71	4547.13 ± 719.86	9600	0.032	0.900	0.944
Multimodal	Volume of parstriangularis R	4150.26 ± 746.18	4224.97 ± 680.93	9028.5	-0.105	0.329	0.469
Multimodal	Volume of pericalcarine L	1983.87 ± 424.20	2216.00 ± 430.23	6615.5	-0.542	<0.001	<0.001*
Multimodal	Volume of pericalcarine R	2163.89 ± 436.12	2350.19 ± 450.45	7479.5	-0.419	0.001	0.003*
Multimodal	Volume of postcentral L	11246.65 ± 1368.98	11922.71 ± 1321.80	-4.19136	-0.502	<0.001	<0.001*
Multimodal	Volume of postcentral R	10750.28 ± 1627.18	11054.16 ± 1283.69	8233	-0.208	0.031	0.072
Multimodal	Volume of posteriorcingulate L	3502.32 ± 496.79	3610.62 ± 556.16	8820	-0.204	0.198	0.327

Multimodal	Volume of posteriorcingulate R	3556.29 ± 480.88	3603.47 ± 479.93	9196.5	-0.098	0.468	0.607
Multimodal	Volume of precentral L	13593.83 ± 1689.92	14421.41 ± 1679.90	-4.09338	-0.490	<0.001	<0.001*
Multimodal	Volume of precentral R	13052.99 ± 1694.42	13818.08 ± 1815.54	7432	-0.433	<0.001	0.002*
Multimodal	Volume of precuneus L	10119.36 ± 1217.36	10436.69 ± 1157.79	7889.5	-0.267	0.008	0.020*
Multimodal	Volume of precuneus R	10807.76 ± 1389.46	11225.35 ± 1370.73	7966	-0.302	0.011	0.027*
Multimodal	Volume of rostralanteriorcingulate L	3654.79 ± 683.32	3759.84 ± 657.04	8505	-0.156	0.079	0.156
Multimodal	Volume of rostralanteriorcingulate R	2656.32 ± 581.79	2644.16 ± 471.53	9361.5	0.023	0.631	0.756
Multimodal	Volume of rostralmiddlefrontal L	11265.34 ± 1746.19	11971.84 ± 1727.34	7453.5	-0.406	<0.001	0.003*
Multimodal	Volume of rostralmiddlefrontal R	11541.19 ± 1649.61	12003.80 ± 1739.75	8087.5	-0.272	0.018	0.043*
Multimodal	Volume of superiorfrontal L	24862.33 ± 3120.01	25852.35 ± 2940.67	7685.5	-0.326	0.003	0.008*
Multimodal	Volume of superiorfrontal R	27701.60 ± 3300.97	28835.93 ± 3312.66	7570.5	-0.342	0.002	0.005*
Multimodal	Volume of superiorparietal L	11294.82 ± 1463.84	11603.60 ± 1548.34	8750	-0.204	0.165	0.280
Multimodal	Volume of superiorparietal R	11428.65 ± 1499.73	11787.88 ± 1526.39	8099.5	-0.237	0.018	0.045*
Multimodal	Volume of superiortemporal L	16758.76 ± 2128.64	17617.46 ± 1789.60	6962	-0.438	<0.001	<0.001*
Multimodal	Volume of superiortemporal R	16000.62 ± 1937.93	16774.45 ± 1583.94	7148	-0.439	<0.001	<0.001*
Multimodal	Volume of supramarginal L	10531.46 ± 1733.95	10952.87 ± 1578.96	8352	-0.254	0.047	0.103
Multimodal	Volume of supramarginal R	10099.55 ± 1525.60	10412.31 ± 1356.30	-1.81272	-0.217	0.071	0.145
Multimodal	Volume of transversetemporal L	1214.78 ± 248.36	1276.49 ± 235.30	7989	-0.255	0.012	0.029*
Multimodal	Volume of transversetemporal R	981.18 ± 183.73	1013.01 ± 167.23	8469	-0.181	0.071	0.144
Multimodal	Mean thickness of caudalanteriorcingulate L	2.71 ± 0.29	2.77 ± 0.25	-1.79184	-0.214	0.074	0.150
Multimodal	Mean thickness of caudalanteriorcingulate R	2.56 ± 0.30	2.53 ± 0.36	9824	0.077	0.837	0.909
Multimodal	Mean thickness of caudalmiddlefrontal L	2.80 ± 0.14	2.92 ± 0.12	4953	-0.945	<0.001	<0.001*
Multimodal	Mean thickness of caudalmiddlefrontal R	2.77 ± 0.13	2.87 ± 0.13	5501	-0.800	<0.001	<0.001*
Multimodal	Mean thickness of cuneus L	1.98 ± 0.13	2.10 ± 0.13	-7.73892	-0.926	<0.001	<0.001*
Multimodal	Mean thickness of cuneus R	1.89 ± 0.12	2.00 ± 0.13	-7.15145	-0.856	<0.001	<0.001*
Multimodal	Mean thickness of entorhinal L	3.18 ± 0.26	3.33 ± 0.26	-4.93804	-0.591	<0.001	<0.001*
Multimodal	Mean thickness of entorhinal R	3.25 ± 0.32	3.40 ± 0.27	-4.14361	-0.496	<0.001	<0.001*
Multimodal	Mean thickness of fusiform L	2.83 ± 0.12	2.93 ± 0.10	5383	-0.905	<0.001	<0.001*
Multimodal	Mean thickness of fusiform R	2.84 ± 0.14	2.93 ± 0.12	-5.61294	-0.672	<0.001	<0.001*
Multimodal	Mean thickness of inferiorparietal L	2.66 ± 0.10	2.75 ± 0.09	4606.5	-1.020	<0.001	<0.001*
Multimodal	Mean thickness of inferiorparietal R	2.69 ± 0.11	2.78 ± 0.11	-6.60033	-0.790	<0.001	<0.001*
Multimodal	Mean thickness of inferiortemporal L	3.00 ± 0.14	3.09 ± 0.14	-5.31645	-0.636	<0.001	<0.001*
Multimodal	Mean thickness of inferiortemporal R	2.96 ± 0.13	3.06 ± 0.14	-6.228	-0.745	<0.001	<0.001*
Multimodal	Mean thickness of insula L	3.13 ± 0.17	3.24 ± 0.15	-5.54122	-0.663	<0.001	<0.001*
Multimodal	Mean thickness of insula R	3.14 ± 0.16	3.23 ± 0.15	-5.13004	-0.614	<0.001	<0.001*
Multimodal	Mean thickness of isthmuscingulate L	2.46 ± 0.18	2.49 ± 0.18	8693	-0.164	0.140	0.248

Multimodal	Mean thickness of isthmuscingulate R	2.51 ± 0.18	2.57 ± 0.20	-2.93212	-0.351	0.004	0.010*
Multimodal	Mean thickness of lateraloccipital L	2.27 ± 0.12	2.36 ± 0.11	-6.49866	-0.778	<0.001	<0.001*
Multimodal	Mean thickness of lateraloccipital R	2.30 ± 0.12	2.39 ± 0.12	-6.29067	-0.753	<0.001	<0.001*
Multimodal	Mean thickness of lateralorbitofrontal L	2.78 ± 0.13	2.88 ± 0.13	5659.5	-0.734	<0.001	<0.001*
Multimodal	Mean thickness of lateralorbitofrontal R	2.79 ± 0.14	2.86 ± 0.12	-4.71186	-0.564	<0.001	<0.001*
Multimodal	Mean thickness of lingual L	1.98 ± 0.14	2.07 ± 0.14	-5.45763	-0.653	<0.001	<0.001*
Multimodal	Mean thickness of lingual R	1.98 ± 0.13	2.03 ± 0.14	-3.26826	-0.391	0.001	0.004*
Multimodal	Mean thickness of medialorbitofrontal L	2.61 ± 0.17	2.68 ± 0.16	7645	-0.373	0.002	0.007*
Multimodal	Mean thickness of medialorbitofrontal R	2.68 ± 0.17	2.68 ± 0.18	-0.31809	-0.038	0.751	0.856
Multimodal	Mean thickness of middletemporal L	2.85 ± 0.15	2.95 ± 0.12	5847	-0.734	<0.001	<0.001*
Multimodal	Mean thickness of middletemporal R	2.92 ± 0.14	3.04 ± 0.13	-7.15442	-0.856	<0.001	<0.001*
Multimodal	Mean thickness of paracentral L	2.64 ± 0.17	2.78 ± 0.16	-6.8182	-0.816	<0.001	<0.001*
Multimodal	Mean thickness of paracentral R	2.62 ± 0.17	2.76 ± 0.16	-7.19445	-0.861	<0.001	<0.001*
Multimodal	Mean thickness of parahippocampal L	2.70 ± 0.26	2.86 ± 0.28	-4.9476	-0.592	<0.001	<0.001*
Multimodal	Mean thickness of parahippocampal R	2.66 ± 0.23	2.74 ± 0.22	7701	-0.380	0.003	0.009*
Multimodal	Mean thickness of parsopercularis L	2.82 ± 0.13	2.92 ± 0.13	-6.713	-0.803	<0.001	<0.001*
Multimodal	Mean thickness of parsopercularis R	2.77 ± 0.12	2.86 ± 0.12	-5.61231	-0.672	<0.001	<0.001*
Multimodal	Mean thickness of parsorbitalis L	2.80 ± 0.14	2.94 ± 0.15	-7.82347	-0.936	<0.001	<0.001*
Multimodal	Mean thickness of parsorbitalis R	2.83 ± 0.18	2.93 ± 0.16	-4.89192	-0.586	<0.001	<0.001*
Multimodal	Mean thickness of parstriangularis L	2.66 ± 0.13	2.76 ± 0.13	5525	-0.809	<0.001	<0.001*
Multimodal	Mean thickness of parstriangularis R	2.63 ± 0.12	2.72 ± 0.13	-5.98928	-0.717	<0.001	<0.001*
Multimodal	Mean thickness of pericalcarine L	1.70 ± 0.13	1.78 ± 0.13	-5.74947	-0.688	<0.001	<0.001*
Multimodal	Mean thickness of pericalcarine R	1.67 ± 0.13	1.73 ± 0.13	-4.34355	-0.520	<0.001	<0.001*
Multimodal	Mean thickness of postcentral L	2.29 ± 0.12	2.40 ± 0.12	-7.87534	-0.943	<0.001	<0.001*
Multimodal	Mean thickness of postcentral R	2.27 ± 0.14	2.36 ± 0.14	6056	-0.649	<0.001	<0.001*
Multimodal	Mean thickness of posteriorcingulate L	2.65 ± 0.18	2.72 ± 0.15	-3.16589	-0.379	0.002	0.005*
Multimodal	Mean thickness of posteriorcingulate R	2.68 ± 0.18	2.73 ± 0.15	-2.47171	-0.296	0.014	0.035*
Multimodal	Mean thickness of precentral L	2.77 ± 0.15	2.90 ± 0.14	4551.5	-0.953	<0.001	<0.001*
Multimodal	Mean thickness of precentral R	2.72 ± 0.15	2.84 ± 0.16	5297	-0.771	<0.001	<0.001*
Multimodal	Mean thickness of precuneus L	2.58 ± 0.12	2.70 ± 0.13	-7.88599	-0.944	<0.001	<0.001*
Multimodal	Mean thickness of precuneus R	2.57 ± 0.11	2.69 ± 0.12	-8.17884	-0.979	<0.001	<0.001*
Multimodal	Mean thickness of rostralanteriorcingulate L	2.87 ± 0.18	2.93 ± 0.16	-3.21373	-0.385	0.001	0.004*
Multimodal	Mean thickness of rostralanteriorcingulate R	2.93 ± 0.20	2.97 ± 0.22	8596.5	-0.218	0.106	0.196
Multimodal	Mean thickness of rostralmiddlefrontal L	2.63 ± 0.11	2.74 ± 0.10	4018	-1.131	<0.001	<0.001*
Multimodal	Mean thickness of rostralmiddlefrontal R	2.60 ± 0.11	2.67 ± 0.09	5673.5	-0.782	<0.001	<0.001*

Multimodal	Mean thickness of superiorfrontal L	2.89 ± 0.12	3.02 ± 0.11	-8.79393	-1.053	<0.001	<0.001*
Multimodal	Mean thickness of superiorfrontal R	2.87 ± 0.11	2.97 ± 0.10	5083.5	-0.881	<0.001	<0.001*
Multimodal	Mean thickness of superiorparietal L	2.43 ± 0.10	2.54 ± 0.11	-9.18254	-1.099	<0.001	<0.001*
Multimodal	Mean thickness of superiorparietal R	2.42 ± 0.11	2.52 ± 0.12	5235	-0.862	<0.001	<0.001*
Multimodal	Mean thickness of superiortemporal L	2.92 ± 0.15	3.05 ± 0.12	4625	-0.979	<0.001	<0.001*
Multimodal	Mean thickness of superiortemporal R	3.00 ± 0.15	3.12 ± 0.14	-6.81602	-0.816	<0.001	<0.001*
Multimodal	Mean thickness of supramarginal L	2.75 ± 0.11	2.88 ± 0.11	-9.56392	-1.145	<0.001	<0.001*
Multimodal	Mean thickness of supramarginal R	2.77 ± 0.12	2.88 ± 0.13	-7.35598	-0.880	<0.001	<0.001*
Multimodal	Mean thickness of transversetemporal L	2.46 ± 0.22	2.58 ± 0.24	-4.58182	-0.548	<0.001	<0.001*
Multimodal	Mean thickness of transversetemporal R	2.52 ± 0.24	2.65 ± 0.28	-4.18925	-0.501	<0.001	<0.001*
Multimodal	Volume of accumbens L	492.31 ± 113.05	525.42 ± 125.69	-2.29953	-0.275	0.022	0.053
Multimodal	Volume of accumbens R	404.90 ± 97.49	427.09 ± 108.51	-1.78579	-0.214	0.075	0.150
Multimodal	Volume of amygdala L	1200.31 ± 225.66	1249.11 ± 214.96	-1.84817	-0.221	0.066	0.135
Multimodal	Volume of amygdala R	1162.88 ± 224.60	1200.75 ± 271.49	-1.25833	-0.151	0.209	0.340
Multimodal	Volume of caudate L	3318.07 ± 390.57	3392.19 ± 402.98	-1.55477	-0.186	0.121	0.219
Multimodal	Volume of caudate R	3452.35 ± 389.47	3546.37 ± 415.80	-1.94021	-0.232	0.053	0.114
Multimodal	Volume of hippocampus L	3717.21 ± 443.90	3899.11 ± 452.14	7491	-0.405	0.001	0.003*
Multimodal	Volume of hippocampus R	3835.84 ± 454.11	3971.57 ± 469.00	-2.4473	-0.293	0.015	0.037*
Multimodal	Volume of pallidum L	1696.65 ± 208.60	1759.60 ± 238.64	-2.32989	-0.279	0.021	0.049*
Multimodal	Volume of pallidum R	1755.58 ± 199.32	1806.06 ± 240.36	8684	-0.227	0.137	0.243
Multimodal	Volume of putamen L	4802.77 ± 576.01	4879.09 ± 550.83	-1.1302	-0.135	0.259	0.392
Multimodal	Volume of putamen R	4829.53 ± 564.52	4926.75 ± 563.42	8812	-0.172	0.194	0.322
Multimodal	Volume of thalamus L	7636.61 ± 748.09	7878.32 ± 756.35	-2.67638	-0.320	0.008	0.020*
Multimodal	Volume of thalamus R	7421.45 ± 732.28	7662.19 ± 757.82	-2.68878	-0.322	0.008	0.020*
Multimodal	Mean FA in anterior corona radiata L	0.45 ± 0.02	0.48 ± 0.02	-9.01439	-1.079	<0.001	<0.001*
Multimodal	Mean FA in anterior corona radiata R	0.46 ± 0.02	0.48 ± 0.03	-8.69809	-1.041	<0.001	<0.001*
Multimodal	Mean FA in anterior limb of internal capsule L	0.58 ± 0.02	0.60 ± 0.02	-7.24793	-0.868	<0.001	<0.001*
Multimodal	Mean FA in anterior limb of internal capsule R	0.59 ± 0.02	0.61 ± 0.02	5633	-0.784	<0.001	<0.001*
Multimodal	Mean FA in body of corpus callosum	0.71 ± 0.02	0.74 ± 0.02	3647	-1.251	<0.001	<0.001*
Multimodal	Mean FA in cerebral peduncle L	0.71 ± 0.02	0.73 ± 0.02	5570	-0.781	<0.001	<0.001*
Multimodal	Mean FA in cerebral peduncle R	0.70 ± 0.02	0.72 ± 0.02	-6.60314	-0.790	<0.001	<0.001*
Multimodal	Mean FA in cingulum cingulate gyrus L	0.61 ± 0.03	0.64 ± 0.03	-8.33037	-0.997	<0.001	<0.001*
Multimodal	Mean FA in cingulum cingulate gyrus R	0.57 ± 0.03	0.60 ± 0.03	-7.46191	-0.893	<0.001	<0.001*
Multimodal	Mean FA in cingulum hippocampus L	0.45 ± 0.03	0.48 ± 0.03	-5.90113	-0.706	<0.001	<0.001*
Multimodal	Mean FA in cingulum hippocampus R	0.45 ± 0.04	0.47 ± 0.04	5924	-0.712	<0.001	<0.001*

Multimodal	Mean FA in corticospinal tract L	0.54 ± 0.03	0.55 ± 0.03	-3.34321	-0.400	<0.001	0.003*
Multimodal	Mean FA in corticospinal tract R	0.52 ± 0.04	0.53 ± 0.04	-2.10409	-0.252	0.036	0.082
Multimodal	Mean FA in external capsule L	0.46 ± 0.02	0.48 ± 0.02	-7.99474	-0.957	<0.001	<0.001*
Multimodal	Mean FA in external capsule R	0.45 ± 0.02	0.47 ± 0.02	-9.28248	-1.111	<0.001	<0.001*
Multimodal	Mean FA in fornix cres+stria terminalis L	0.52 ± 0.03	0.55 ± 0.03	5523	-0.790	<0.001	<0.001*
Multimodal	Mean FA in fornix cres+stria terminalis R	0.52 ± 0.03	0.55 ± 0.03	5659.5	-0.771	<0.001	<0.001*
Multimodal	Mean FA in fornix	0.45 ± 0.08	0.49 ± 0.06	6981	-0.507	<0.001	<0.001*
Multimodal	Mean FA in genu of corpus callosum	0.72 ± 0.03	0.75 ± 0.02	3167	-1.322	<0.001	<0.001*
Multimodal	Mean FA in inferior cerebellar peduncle L	0.54 ± 0.03	0.56 ± 0.03	6850	-0.513	<0.001	<0.001*
Multimodal	Mean FA in inferior cerebellar peduncle R	0.55 ± 0.03	0.56 ± 0.02	6527	-0.599	<0.001	<0.001*
Multimodal	Mean FA in medial lemniscus L	0.58 ± 0.02	0.59 ± 0.03	6544	-0.554	<0.001	<0.001*
Multimodal	Mean FA in medial lemniscus R	0.59 ± 0.02	0.60 ± 0.02	-4.53306	-0.543	<0.001	<0.001*
Multimodal	Mean FA in middle cerebellar peduncle	0.54 ± 0.02	0.55 ± 0.02	6243	-0.662	<0.001	<0.001*
Multimodal	Mean FA in pontine crossing tract	0.41 ± 0.03	0.41 ± 0.03	8616	-0.169	0.112	0.204
Multimodal	Mean FA in posterior corona radiata L	0.47 ± 0.02	0.49 ± 0.02	3995	-1.180	<0.001	<0.001*
Multimodal	Mean FA in posterior corona radiata R	0.48 ± 0.02	0.51 ± 0.02	-10.51	-1.258	<0.001	<0.001*
Multimodal	Mean FA in posterior limb of internal capsule L	0.68 ± 0.02	0.69 ± 0.02	-5.19389	-0.622	<0.001	<0.001*
Multimodal	Mean FA in posterior limb of internal capsule R	0.67 ± 0.02	0.69 ± 0.02	-5.88294	-0.704	<0.001	<0.001*
Multimodal	Mean FA in posterior thalamic radiation L	0.59 ± 0.03	0.62 ± 0.03	4282	-1.044	<0.001	<0.001*
Multimodal	Mean FA in posterior thalamic radiation R	0.58 ± 0.03	0.61 ± 0.03	-9.37518	-1.122	<0.001	<0.001*
Multimodal	Mean FA in retrolenticular part of internal capsule L	0.61 ± 0.02	0.63 ± 0.02	-7.67162	-0.918	<0.001	<0.001*
Multimodal	Mean FA in retrolenticular part of internal capsule R	0.58 ± 0.03	0.60 ± 0.02	-7.17906	-0.859	<0.001	<0.001*
Multimodal	Mean FA in sagittal stratum L	0.56 ± 0.03	0.58 ± 0.02	-7.89334	-0.945	<0.001	<0.001*
Multimodal	Mean FA in sagittal stratum R	0.55 ± 0.03	0.58 ± 0.02	4387	-1.016	<0.001	<0.001*
Multimodal	Mean FA in splenium of corpus callosum	0.78 ± 0.02	0.80 ± 0.02	-9.59613	-1.149	<0.001	<0.001*
Multimodal	Mean FA in superior cerebellar peduncle L	0.70 ± 0.02	0.71 ± 0.03	-4.07562	-0.488	<0.001	<0.001*
Multimodal	Mean FA in superior cerebellar peduncle R	0.69 ± 0.02	0.70 ± 0.03	-3.86753	-0.463	<0.001	<0.001*
Multimodal	Mean FA in superior corona radiata L	0.48 ± 0.02	0.50 ± 0.02	-10.2062	-1.222	<0.001	<0.001*
Multimodal	Mean FA in superior corona radiata R	0.48 ± 0.02	0.50 ± 0.02	-9.12148	-1.092	<0.001	<0.001*
Multimodal	Mean FA in superior fronto-occipital fasciculus L	0.46 ± 0.03	0.48 ± 0.03	-5.88921	-0.705	<0.001	<0.001*
Multimodal	Mean FA in superior fronto-occipital fasciculus R	0.45 ± 0.03	0.47 ± 0.03	-5.12451	-0.613	<0.001	<0.001*
Multimodal	Mean FA in superior longitudinal fasciculus L	0.52 ± 0.02	0.54 ± 0.02	-7.67906	-0.919	<0.001	<0.001*
Multimodal	Mean FA in superior longitudinal fasciculus R	0.51 ± 0.02	0.53 ± 0.02	-8.1403	-0.974	<0.001	<0.001*
Multimodal	Mean FA in tapetum L	0.58 ± 0.06	0.61 ± 0.06	-3.71243	-0.444	<0.001	<0.001*
Multimodal	Mean FA in tapetum R	0.55 ± 0.06	0.58 ± 0.05	-4.63901	-0.555	<0.001	<0.001*
Multimodal	Mean FA in uncinate fasciculus L	0.50 ± 0.04	0.52 ± 0.03	6733	-0.543	<0.001	<0.001*

Multimodal	Mean FA in uncinate fasciculus R	0.52 ± 0.04	0.54 ± 0.03	6708	-0.560	<0.001	<0.001*
Multimodal	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	7.11151	0.851	<0.001	<0.001*
Multimodal	Mean AD in anterior corona radiata R	0.12 ± 0.00	0.12 ± 0.00	6.710392	0.803	<0.001	<0.001*
Multimodal	Mean AD in anterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	2.063889	0.247	0.040	0.089
Multimodal	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	10764	0.228	0.109	0.201
Multimodal	Mean AD in body of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	12211	0.484	<0.001	<0.001*
Multimodal	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	-0.30026	-0.036	0.764	0.870
Multimodal	Mean AD in cerebral peduncle R	0.14 ± 0.01	0.14 ± 0.01	10036	0.037	0.602	0.735
Multimodal	Mean AD in cingulum cingulate gyrus L	0.14 ± 0.01	0.14 ± 0.01	1.003364	0.120	0.317	0.458
Multimodal	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	1.245403	0.149	0.214	0.345
Multimodal	Mean AD in cingulum hippocampus L	0.12 ± 0.01	0.12 ± 0.00	11383.5	0.284	0.012	0.029*
Multimodal	Mean AD in cingulum hippocampus R	0.12 ± 0.01	0.12 ± 0.01	1.897787	0.227	0.059	0.125
Multimodal	Mean AD in corticospinal tract L	0.13 ± 0.01	0.13 ± 0.01	10464.5	0.102	0.247	0.380
Multimodal	Mean AD in corticospinal tract R	0.13 ± 0.01	0.13 ± 0.01	10358	0.157	0.317	0.458
Multimodal	Mean AD in external capsule L	0.12 ± 0.00	0.12 ± 0.00	3.146602	0.377	0.002	0.005*
Multimodal	Mean AD in external capsule R	0.12 ± 0.00	0.12 ± 0.00	4.774337	0.571	<0.001	<0.001*
Multimodal	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.14 ± 0.00	10487	0.097	0.233	0.366
Multimodal	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	10248.5	0.091	0.402	0.540
Multimodal	Mean AD in fornix	0.23 ± 0.02	0.22 ± 0.02	11602	0.393	0.004	0.012*
Multimodal	Mean AD in genu of corpus callosum	0.16 ± 0.01	0.15 ± 0.00	3.861998	0.462	<0.001	<0.001*
Multimodal	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.00	0.12 ± 0.00	1.862396	0.223	0.064	0.132
Multimodal	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.00	0.12 ± 0.00	0.858295	0.103	0.391	0.529
Multimodal	Mean AD in medial lemniscus L	0.13 ± 0.01	0.13 ± 0.01	8984.5	-0.107	0.298	0.439
Multimodal	Mean AD in medial lemniscus R	0.14 ± 0.01	0.13 ± 0.01	9844	0.057	0.814	0.897
Multimodal	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	0.65369	0.078	0.514	0.659
Multimodal	Mean AD in pontine crossing tract	0.12 ± 0.01	0.12 ± 0.01	9754.5	0.063	0.918	0.955
Multimodal	Mean AD in posterior corona radiata L	0.13 ± 0.01	0.12 ± 0.00	14047	0.872	<0.001	<0.001*
Multimodal	Mean AD in posterior corona radiata R	0.13 ± 0.01	0.13 ± 0.00	13739.5	0.781	<0.001	<0.001*
Multimodal	Mean AD in posterior limb of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	1.396218	0.167	0.164	0.280
Multimodal	Mean AD in posterior limb of internal capsule R	0.14 ± 0.00	0.14 ± 0.00	1.789951	0.214	0.075	0.150
Multimodal	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	3.241851	0.388	0.001	0.004*
Multimodal	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.01	12022	0.415	<0.001	0.002*
Multimodal	Mean AD in retrolenticular part of internal capsule L	0.14 ± 0.00	0.14 ± 0.00	2.529605	0.303	0.012	0.030*
Multimodal	Mean AD in retrolenticular part of internal capsule R	0.14 ± 0.01	0.13 ± 0.00	4.716898	0.565	<0.001	<0.001*
Multimodal	Mean AD in sagittal stratum L	0.14 ± 0.01	0.13 ± 0.01	4.153878	0.497	<0.001	<0.001*

Multimodal	Mean AD in sagittal stratum R	0.14 ± 0.01	0.14 ± 0.01	4.35126	0.521	<0.001	<0.001*
Multimodal	Mean AD in splenium of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	4.064887	0.487	<0.001	<0.001*
Multimodal	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	10880	0.201	0.076	0.150
Multimodal	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	0.852501	0.102	0.395	0.532
Multimodal	Mean AD in superior corona radiata L	0.12 ± 0.00	0.11 ± 0.00	12952	0.589	<0.001	<0.001*
Multimodal	Mean AD in superior corona radiata R	0.12 ± 0.00	0.11 ± 0.00	5.028614	0.602	<0.001	<0.001*
Multimodal	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.01	0.11 ± 0.01	11635	0.349	0.004	0.010*
Multimodal	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.11 ± 0.01	11233.5	0.254	0.021	0.051
Multimodal	Mean AD in superior longitudinal fasciculus L	0.12 ± 0.00	0.12 ± 0.00	5.465035	0.654	<0.001	<0.001*
Multimodal	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	5.455565	0.653	<0.001	<0.001*
Multimodal	Mean AD in tapetum L	0.16 ± 0.02	0.16 ± 0.01	10989	0.274	0.053	0.112
Multimodal	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	12057	0.407	<0.001	0.001*
Multimodal	Mean AD in uncinate fasciculus L	0.12 ± 0.01	0.12 ± 0.01	2.156298	0.258	0.032	0.074
Multimodal	Mean AD in uncinate fasciculus R	0.12 ± 0.00	0.12 ± 0.00	10342.5	0.134	0.328	0.469
Multimodal	Mean RD in anterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	16525	1.432	<0.001	<0.001*
Multimodal	Mean RD in anterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	16534	1.447	<0.001	<0.001*
Multimodal	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	14686.5	0.930	<0.001	<0.001*
Multimodal	Mean RD in anterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	14143.5	0.809	<0.001	<0.001*
Multimodal	Mean RD in body of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	16438.5	1.434	<0.001	<0.001*
Multimodal	Mean RD in cerebral peduncle L	0.04 ± 0.00	0.03 ± 0.00	13707	0.745	<0.001	<0.001*
Multimodal	Mean RD in cerebral peduncle R	0.04 ± 0.00	0.03 ± 0.00	13665	0.760	<0.001	<0.001*
Multimodal	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.04 ± 0.00	10.32254	1.236	<0.001	<0.001*
Multimodal	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.05 ± 0.00	9.79642	1.173	<0.001	<0.001*
Multimodal	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.05 ± 0.00	7.685148	0.920	<0.001	<0.001*
Multimodal	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.05 ± 0.00	14664.5	0.936	<0.001	<0.001*
Multimodal	Mean RD in corticospinal tract L	0.05 ± 0.01	0.05 ± 0.01	11193	0.264	0.025	0.059
Multimodal	Mean RD in corticospinal tract R	0.06 ± 0.01	0.05 ± 0.01	10787	0.225	0.101	0.190
Multimodal	Mean RD in external capsule L	0.05 ± 0.00	0.05 ± 0.00	8.674881	1.038	<0.001	<0.001*
Multimodal	Mean RD in external capsule R	0.06 ± 0.00	0.05 ± 0.00	15642.5	1.190	<0.001	<0.001*
Multimodal	Mean RD in fornix cres+stria terminalis L	0.06 ± 0.00	0.05 ± 0.00	13814.5	0.788	<0.001	<0.001*
Multimodal	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.00	0.06 ± 0.00	13757.5	0.776	<0.001	<0.001*
Multimodal	Mean RD in fornix	0.11 ± 0.03	0.10 ± 0.02	12104.5	0.440	<0.001	0.001*
Multimodal	Mean RD in genu of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	16407.5	1.342	<0.001	<0.001*
Multimodal	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	13450.5	0.710	<0.001	<0.001*
Multimodal	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	13294.5	0.706	<0.001	<0.001*
Multimodal	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	11630.5	0.294	0.004	0.010*

Multimodal	Mean RD in medial lemniscus R	0.05 ± 0.00	0.05 ± 0.00	11974	0.401	<0.001	0.002*
Multimodal	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	12681.5	0.572	<0.001	<0.001*
Multimodal	Mean RD in pontine crossing tract	0.06 ± 0.01	0.06 ± 0.01	9839	0.090	0.819	0.902
Multimodal	Mean RD in posterior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	16730	1.462	<0.001	<0.001*
Multimodal	Mean RD in posterior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	16786.5	1.456	<0.001	<0.001*
Multimodal	Mean RD in posterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	6.415874	0.768	<0.001	<0.001*
Multimodal	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	7.385974	0.884	<0.001	<0.001*
Multimodal	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.00	15473.5	1.073	<0.001	<0.001*
Multimodal	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	15960.5	1.284	<0.001	<0.001*
Multimodal	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.00	0.04 ± 0.00	9.584396	1.147	<0.001	<0.001*
Multimodal	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	15550.5	1.194	<0.001	<0.001*
Multimodal	Mean RD in sagittal stratum L	0.05 ± 0.00	0.05 ± 0.00	15646	1.220	<0.001	<0.001*
Multimodal	Mean RD in sagittal stratum R	0.05 ± 0.00	0.05 ± 0.00	15738	1.219	<0.001	<0.001*
Multimodal	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.03 ± 0.00	11.70678	1.401	<0.001	<0.001*
Multimodal	Mean RD in superior cerebellar peduncle L	0.04 ± 0.00	0.04 ± 0.00	4.783305	0.573	<0.001	<0.001*
Multimodal	Mean RD in superior cerebellar peduncle R	0.04 ± 0.00	0.04 ± 0.00	4.096536	0.490	<0.001	<0.001*
Multimodal	Mean RD in superior corona radiata L	0.05 ± 0.00	0.05 ± 0.00	16827.5	1.565	<0.001	<0.001*
Multimodal	Mean RD in superior corona radiata R	0.05 ± 0.00	0.05 ± 0.00	16777	1.567	<0.001	<0.001*
Multimodal	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.00	0.05 ± 0.00	14186	0.732	<0.001	<0.001*
Multimodal	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.00	0.05 ± 0.00	13985.5	0.746	<0.001	<0.001*
Multimodal	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	10.36235	1.240	<0.001	<0.001*
Multimodal	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.00	0.05 ± 0.00	10.73614	1.285	<0.001	<0.001*
Multimodal	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	11979.5	0.461	<0.001	0.002*
Multimodal	Mean RD in tapetum R	0.07 ± 0.01	0.06 ± 0.01	12920.5	0.587	<0.001	<0.001*
Multimodal	Mean RD in uncinate fasciculus L	0.05 ± 0.00	0.05 ± 0.00	13733	0.734	<0.001	<0.001*
Multimodal	Mean RD in uncinate fasciculus R	0.05 ± 0.00	0.05 ± 0.00	13480.5	0.708	<0.001	<0.001*
Multimodal	Median z-statistic (amygdala) for faces-shapes contrast	1.18 ± 0.85	1.30 ± 0.92	-1.05334	-0.126	0.293	0.433
Multimodal	Median z-statistic for faces activation	2.63 ± 1.22	2.92 ± 1.34	-1.86111	-0.223	0.064	0.132
Multimodal	Median z-statistic for shapes activation	2.45 ± 1.22	2.72 ± 1.36	8591	-0.215	0.104	0.194
Multimodal	Median z-statistic for faces-shapes contrast	2.49 ± 1.47	2.66 ± 1.32	-0.97993	-0.117	0.328	0.469
Multimodal	90th percentile of z-statistic (amygdala) for faces-shapes contrast	2.92 ± 1.01	3.05 ± 1.12	-1.03934	-0.124	0.300	0.439
Multimodal	90th percentile of z-statistic for faces activation	6.05 ± 1.85	6.38 ± 1.77	8723	-0.186	0.153	0.265
Multimodal	90th percentile of z-statistic for shapes activation	5.49 ± 1.75	5.80 ± 1.77	8923	-0.174	0.257	0.391
Multimodal	90th percentile of z-statistic for faces-shapes contrast	6.05 ± 2.22	6.23 ± 1.87	9118.5	-0.089	0.400	0.538
Multimodal	Left amygdala habituation for faces condition	0.02 ± 0.31	0.08 ± 0.28	8853	-0.199	0.216	0.346

Multimodal	Right amygdala habituation for faces condition	0.02 ± 0.31	0.07 ± 0.24	9149	-0.161	0.426	0.565
Multimodal	Left amygdala habituation for shapes condition	0.01 ± 0.35	0.07 ± 0.26	8724	-0.210	0.153	0.265
Multimodal	Right amygdala habituation for shapes condition	0.05 ± 0.32	0.06 ± 0.23	9365	-0.028	0.635	0.759
Multimodal	Spos_1	13.08 ± 4.01	12.27 ± 3.85	10832	0.206	0.088	0.169
Multimodal	Spos_2	24.71 ± 4.38	25.35 ± 4.05	-1.26134	-0.151	0.208	0.339
Multimodal	Spos_3	15.43 ± 4.02	15.39 ± 4.29	10041	0.011	0.597	0.732
Multimodal	Spos_4	23.86 ± 4.61	23.08 ± 4.57	1.422226	0.170	0.156	0.269
Multimodal	Spos_5	28.49 ± 3.56	29.17 ± 3.60	8537	-0.189	0.088	0.169
Multimodal	Spos_6	14.09 ± 3.75	14.12 ± 3.83	9615	-0.010	0.918	0.955
Multimodal	Spos_7	21.27 ± 4.71	21.55 ± 3.97	-0.54863	-0.066	0.584	0.721
Multimodal	Spos_8	18.90 ± 4.57	18.93 ± 5.13	9873	-0.008	0.780	0.881
Multimodal	Spos_9	18.72 ± 3.88	19.15 ± 3.91	8850	-0.108	0.214	0.345
Multimodal	Spos_10	24.48 ± 3.54	24.25 ± 4.06	0.500793	0.060	0.617	0.746
Multimodal	Spos_11	31.00 ± 3.92	31.30 ± 3.94	-0.63648	-0.076	0.525	0.669
Multimodal	Spos_12	26.79 ± 3.27	27.42 ± 3.26	-1.61098	-0.193	0.108	0.201
Multimodal	Spos_13	22.26 ± 3.72	23.01 ± 3.90	-1.63245	-0.195	0.104	0.194
Multimodal	Spos_14	19.09 ± 3.89	19.31 ± 4.45	9544	-0.052	0.834	0.909
Multimodal	Spos_15	19.43 ± 3.95	20.58 ± 4.07	-2.38152	-0.285	0.018	0.044*
Multimodal	Spos_16	12.00 ± 4.83	11.90 ± 4.41	9719	0.021	0.960	0.971
Multimodal	Spos_17	13.63 ± 3.38	13.77 ± 3.76	9599	-0.039	0.899	0.944
Multimodal	Spos_18	23.22 ± 4.13	23.80 ± 3.97	-1.19135	-0.143	0.235	0.367
Multimodal	Spos_19	21.84 ± 3.69	23.02 ± 3.58	-2.69846	-0.323	0.007	0.019*
Multimodal	Spos_20	13.47 ± 3.70	13.39 ± 3.46	0.196837	0.024	0.844	0.912
Multimodal	Spos_21	22.42 ± 3.67	23.20 ± 3.59	-1.77854	-0.213	0.076	0.151
Multimodal	Spos_22	17.77 ± 4.31	18.53 ± 3.88	8558	-0.186	0.094	0.177
Multimodal	Spos_23	11.37 ± 3.26	11.88 ± 3.71	8926	-0.144	0.259	0.392
Multimodal	Spos_24	31.67 ± 3.75	32.08 ± 4.10	-0.8617	-0.103	0.390	0.528
Multimodal	Spos_25	23.59 ± 3.89	25.02 ± 4.41	-2.87107	-0.344	0.004	0.012*
Multimodal	Spos_26	22.90 ± 3.58	23.12 ± 3.59	-0.50844	-0.061	0.612	0.743
Multimodal	Spos_27	18.20 ± 4.24	19.22 ± 4.42	-1.9552	-0.234	0.052	0.111
Multimodal	Spos_28	19.73 ± 3.55	20.36 ± 4.12	8873	-0.164	0.227	0.360
Multimodal	Spos_29	27.65 ± 4.27	27.52 ± 4.29	0.247272	0.030	0.805	0.889
Multimodal	Spos_30	12.11 ± 3.35	12.49 ± 3.39	9089	-0.111	0.376	0.516
Multimodal	Spos_31	27.61 ± 4.33	28.48 ± 4.30	-1.69264	-0.203	0.092	0.174
Multimodal	Spos_32	13.92 ± 3.73	14.22 ± 3.50	9102	-0.083	0.386	0.526
Multimodal	Spos_33	20.63 ± 3.61	22.27 ± 3.73	-3.72421	-0.446	<0.001	<0.001*
Multimodal	Spos_34	18.43 ± 3.07	18.07 ± 3.21	0.94303	0.113	0.346	0.487
Multimodal	Spos_35	17.03 ± 3.63	18.02 ± 4.09	8508	-0.256	0.080	0.157
Multimodal	Spos_36	24.12 ± 3.52	23.23 ± 3.72	2.050638	0.245	0.041	0.091
Multimodal	Spos_37	26.58 ± 4.10	27.88 ± 3.78	7722	-0.330	0.004	0.010*
Multimodal	Spos_38	12.19 ± 3.61	12.39 ± 3.39	9125	-0.059	0.405	0.542
Multimodal	Spos_39	31.24 ± 3.48	31.18 ± 3.54	0.14427	0.017	0.885	0.937
Multimodal	Spos_40	18.50 ± 4.31	18.75 ± 3.87	9262	-0.061	0.530	0.673

Multimodal	Spos_41	19.20 ± 5.00	19.61 ± 4.65	8901	-0.086	0.244	0.379
Multimodal	Spos_42	19.07 ± 3.77	19.09 ± 3.63	-0.05708	-0.007	0.955	0.969
Multimodal	Spos_43	9.60 ± 2.80	9.56 ± 2.80	9698	0.015	0.985	0.987
Multimodal	Spos_44	22.52 ± 4.08	23.90 ± 4.19	-2.7663	-0.331	0.006	0.016*
Multimodal	Spos_45	20.14 ± 4.20	21.68 ± 4.00	-3.13986	-0.376	0.002	0.005*
Multimodal	Spos_46	16.97 ± 4.33	17.21 ± 4.14	-0.46965	-0.056	0.639	0.762
Multimodal	Spos_47	21.30 ± 4.51	22.26 ± 4.19	-1.85309	-0.222	0.065	0.134
Multimodal	Spos_48	21.98 ± 3.45	22.24 ± 3.56	-0.59655	-0.071	0.551	0.694
Multimodal	Spos_49	30.16 ± 4.35	29.75 ± 4.48	10333	0.093	0.335	0.474
Multimodal	Spos_50	11.57 ± 2.85	12.11 ± 3.21	8827	-0.176	0.202	0.332
Multimodal	Spos_51	11.82 ± 2.93	11.94 ± 2.89	9361	-0.044	0.630	0.756
Multimodal	Spos_52	12.11 ± 3.12	12.25 ± 2.97	9319	-0.045	0.587	0.721
Multimodal	Spos_53	13.50 ± 3.71	14.07 ± 3.81	8853	-0.152	0.216	0.346
Multimodal	Spos_54	11.50 ± 2.95	11.55 ± 2.65	-0.16006	-0.019	0.873	0.933
Multimodal	Spos_55	9.49 ± 2.22	9.93 ± 2.27	8652	-0.193	0.125	0.224
Multimodal	Sneg_1	18.26 ± 6.55	17.21 ± 5.87	10646	0.170	0.153	0.265
Multimodal	Sneg_2	28.37 ± 4.49	28.31 ± 4.11	0.120376	0.014	0.904	0.945
Multimodal	Sneg_3	18.75 ± 4.80	19.29 ± 4.52	-0.97333	-0.116	0.331	0.471
Multimodal	Sneg_4	27.11 ± 6.30	26.55 ± 6.49	0.734786	0.088	0.463	0.604
Multimodal	Sneg_5	28.59 ± 4.68	28.82 ± 4.23	-0.43027	-0.051	0.667	0.782
Multimodal	Sneg_6	20.47 ± 7.81	20.40 ± 7.42	9571	0.009	0.866	0.928
Multimodal	Sneg_7	22.71 ± 4.55	23.17 ± 4.61	8978	-0.102	0.293	0.433
Multimodal	Sneg_8	19.03 ± 6.60	19.15 ± 6.59	9506	-0.018	0.791	0.886
Multimodal	Sneg_9	19.80 ± 3.99	19.77 ± 4.35	9743	0.005	0.932	0.961
Multimodal	Sneg_10	25.72 ± 5.46	24.97 ± 4.74	1.220196	0.146	0.223	0.355
Multimodal	Sneg_11	27.35 ± 4.10	27.68 ± 3.96	9564	-0.081	0.858	0.923
Multimodal	Sneg_12	30.37 ± 5.42	30.73 ± 4.91	-0.58661	-0.070	0.558	0.699
Multimodal	Sneg_13	22.09 ± 3.93	23.09 ± 4.49	-1.97861	-0.237	0.049	0.105
Multimodal	Sneg_14	24.47 ± 6.09	23.69 ± 5.46	1.117128	0.134	0.265	0.398
Multimodal	Sneg_15	22.10 ± 4.17	23.21 ± 4.45	-2.14519	-0.257	0.033	0.075
Multimodal	Sneg_16	14.68 ± 7.24	13.86 ± 6.54	10209	0.119	0.436	0.575
Multimodal	Sneg_17	18.27 ± 3.03	19.29 ± 3.58	8115	-0.304	0.020	0.047*
Multimodal	Sneg_18	25.85 ± 5.14	27.04 ± 4.85	-1.98383	-0.237	0.048	0.104
Multimodal	Sneg_19	23.63 ± 4.81	24.03 ± 5.16	-0.66869	-0.080	0.504	0.649
Multimodal	Sneg_20	17.93 ± 5.08	18.42 ± 6.09	9374	-0.086	0.644	0.763
Multimodal	Sneg_21	21.34 ± 3.84	21.48 ± 4.23	-0.29663	-0.036	0.767	0.870
Multimodal	Sneg_22	17.37 ± 4.35	18.30 ± 4.47	8502	-0.209	0.079	0.155
Multimodal	Sneg_23	16.59 ± 3.36	16.64 ± 3.68	9863	-0.015	0.792	0.886
Multimodal	Sneg_24	28.24 ± 4.66	28.02 ± 3.92	9870	0.050	0.784	0.882
Multimodal	Sneg_25	21.77 ± 4.60	22.76 ± 4.32	-1.86411	-0.223	0.063	0.132
Multimodal	Sneg_26	25.52 ± 4.47	25.57 ± 4.62	9379	-0.011	0.650	0.768
Multimodal	Sneg_27	20.86 ± 3.70	22.26 ± 4.08	-2.98921	-0.358	0.003	0.009*
Multimodal	Sneg_28	21.99 ± 5.37	22.53 ± 5.93	-0.78943	-0.094	0.431	0.570
Multimodal	Sneg_29	23.27 ± 4.72	23.04 ± 5.00	0.387849	0.046	0.698	0.807

Multimodal	Sneg_30	16.56 ± 5.76	16.80 ± 5.44	9314	-0.044	0.582	0.720
Multimodal	Sneg_31	24.38 ± 4.47	24.51 ± 4.12	9598	-0.032	0.898	0.944
Multimodal	Sneg_32	16.63 ± 6.52	16.95 ± 5.60	9005	-0.052	0.312	0.455
Multimodal	Sneg_33	21.78 ± 4.59	22.82 ± 4.71	-1.87435	-0.224	0.062	0.130
Multimodal	Sneg_34	24.53 ± 4.50	25.29 ± 4.95	9080	-0.161	0.369	0.510
Multimodal	Sneg_35	17.64 ± 3.61	18.73 ± 3.99	8306	-0.284	0.040	0.089
Multimodal	Sneg_36	25.21 ± 4.48	24.85 ± 4.16	10190	0.083	0.453	0.593
Multimodal	Sneg_37	24.87 ± 4.32	25.82 ± 4.51	-1.78591	-0.214	0.075	0.150
Multimodal	Sneg_38	12.76 ± 3.01	13.09 ± 3.37	9086	-0.104	0.373	0.515
Multimodal	Sneg_39	27.28 ± 5.18	27.83 ± 4.80	-0.91451	-0.109	0.361	0.502
Multimodal	Sneg_40	22.11 ± 4.10	22.24 ± 3.44	9437	-0.033	0.713	0.820
Multimodal	Sneg_41	19.34 ± 5.93	19.49 ± 5.43	9311	-0.026	0.579	0.718
Multimodal	Sneg_42	21.59 ± 4.66	21.47 ± 4.11	0.217297	0.026	0.828	0.907
Multimodal	Sneg_43	16.21 ± 4.11	17.00 ± 3.67	8284	-0.205	0.037	0.083
Multimodal	Sneg_44	21.10 ± 3.83	22.62 ± 3.71	-3.37583	-0.404	<0.001	0.003*
Multimodal	Sneg_45	18.31 ± 4.14	18.59 ± 3.78	9216	-0.070	0.486	0.628
Multimodal	Sneg_46	18.47 ± 3.35	18.65 ± 3.45	9637	-0.050	0.944	0.963
Multimodal	Sneg_47	16.86 ± 4.45	17.36 ± 4.32	8927	-0.114	0.260	0.392
Multimodal	Sneg_48	20.82 ± 4.37	20.52 ± 4.07	0.575293	0.069	0.566	0.707
Multimodal	Sneg_49	19.44 ± 3.48	19.34 ± 4.24	10031	0.024	0.607	0.739
Multimodal	Sneg_50	15.97 ± 3.26	15.88 ± 3.51	9968	0.029	0.674	0.787
Multimodal	Sneg_51	17.62 ± 3.90	17.53 ± 3.47	0.200045	0.024	0.842	0.911
Multimodal	Sneg_52	16.85 ± 3.68	16.64 ± 3.26	0.500945	0.060	0.617	0.746
Multimodal	Sneg_53	13.73 ± 3.91	14.40 ± 4.07	8578	-0.166	0.100	0.188
Multimodal	Sneg_54	15.06 ± 3.54	15.64 ± 4.27	8834	-0.146	0.206	0.337
Multimodal	Sneg_55	11.26 ± 2.41	10.86 ± 2.00	10336	0.185	0.333	0.472
Multimodal	ADHD Demontis2022	0.37 ± 0.62	0.36 ± 0.53	9787	0.003	0.880	0.935
Multimodal	ALCDEP Walters2018	-1.12 ± 0.22	-1.12 ± 0.25	9852	0.000	0.804	0.889
Multimodal	AN Watson2019	-4.30 ± 0.62	-4.27 ± 0.74	9517	-0.048	0.803	0.889
Multimodal	ASD Grove2019	-0.32 ± 0.36	-0.33 ± 0.40	0.211289	0.025	0.833	0.909
Multimodal	BD PGC4 2025	-1.31 ± 0.56	-1.48 ± 0.55	2.59022	0.310	0.010	0.026*
Multimodal	BMI Locke2015	0.35 ± 0.19	0.32 ± 0.24	10493	0.139	0.230	0.363
Multimodal	bNGF Konieczny2025	-0.01 ± 0.03	-0.01 ± 0.04	0.727765	0.087	0.467	0.607
Multimodal	CAD Nikpay2015	0.93 ± 0.41	0.93 ± 0.45	0.119077	0.014	0.905	0.945
Multimodal	CCL11 Konieczny2025	-0.77 ± 0.26	-0.81 ± 0.23	10432	0.166	0.267	0.400
Multimodal	CCL2 Konieczny2025	0.28 ± 0.55	0.25 ± 0.54	9988	0.048	0.653	0.770
Multimodal	CCL3 Konieczny2025	-0.43 ± 0.31	-0.46 ± 0.33	0.86493	0.104	0.388	0.527
Multimodal	CCL4 Konieczny2025	0.52 ± 0.39	0.57 ± 0.41	8655	-0.126	0.126	0.225
Multimodal	CCL7 Konieczny2025	-0.96 ± 0.37	-0.91 ± 0.36	9022	-0.145	0.324	0.467
Multimodal	CRP Said2022	0.31 ± 0.42	0.36 ± 0.36	8958	-0.135	0.280	0.416
Multimodal	CSF1 Konieczny2025	0.66 ± 0.67	0.70 ± 0.63	-0.4989	-0.060	0.618	0.746
Multimodal	CSF3 Konieczny2025	0.48 ± 0.31	0.47 ± 0.31	9634	0.007	0.940	0.962
Multimodal	CTACK Konieczny2025	-0.04 ± 0.05	-0.04 ± 0.05	0.293297	0.035	0.770	0.870
Multimodal	CUD Johnson2020	-1.16 ± 0.36	-1.10 ± 0.35	8903	-0.169	0.245	0.379

Multimodal	CXCL1 Konieczny2025	-3.32 ± 0.73	-3.49 ± 0.85	10847	0.215	0.084	0.163
Multimodal	CXCL10 Konieczny2025	-0.09 ± 0.11	-0.09 ± 0.10	9673	0.020	0.986	0.987
Multimodal	CXCL12 Konieczny2025	0.18 ± 0.13	0.16 ± 0.14	1.297231	0.155	0.196	0.324
Multimodal	CXCL9 Konieczny2025	-0.01 ± 0.08	-0.02 ± 0.09	1.164891	0.139	0.245	0.379
Multimodal	FGFb Konieczny2025	0.57 ± 0.35	0.53 ± 0.39	10451	0.104	0.255	0.391
Multimodal	GAD FinnGen2024	0.14 ± 0.28	0.12 ± 0.27	0.562142	0.067	0.574	0.715
Multimodal	HbA1c Willems2023	0.12 ± 0.07	0.12 ± 0.07	9432	-0.109	0.707	0.816
Multimodal	HDL Graham2021	1.90 ± 0.45	1.84 ± 0.43	10718	0.140	0.125	0.224
Multimodal	HGF Konieczny2025	0.36 ± 0.14	0.36 ± 0.13	-0.34172	-0.041	0.733	0.838
Multimodal	IFNg Konieczny2025	0.10 ± 0.10	0.09 ± 0.10	10225	0.103	0.422	0.564
Multimodal	IL10 Konieczny2025	0.05 ± 0.05	0.03 ± 0.05	2.107167	0.252	0.036	0.082
Multimodal	IL13 Konieczny2025	-0.01 ± 0.09	-0.02 ± 0.10	1.093463	0.131	0.275	0.410
Multimodal	IL16 Konieczny2025	0.31 ± 0.46	0.31 ± 0.45	9657	0.008	0.967	0.977
Multimodal	IL17 Konieczny2025	0.06 ± 0.04	0.06 ± 0.05	10888	0.180	0.074	0.150
Multimodal	IL18 Konieczny2025	1.26 ± 1.15	1.27 ± 1.10	9773	-0.009	0.896	0.944
Multimodal	IL1b Konieczny2025	-0.76 ± 0.18	-0.78 ± 0.16	0.97815	0.117	0.329	0.469
Multimodal	IL1RA Konieczny2025	-0.28 ± 0.18	-0.29 ± 0.17	0.295027	0.035	0.768	0.870
Multimodal	IL2 Konieczny2025	0.18 ± 0.07	0.17 ± 0.07	0.884888	0.106	0.377	0.516
Multimodal	IL2RA Konieczny2025	0.09 ± 0.07	0.08 ± 0.06	1.039891	0.124	0.299	0.439
Multimodal	IL4 Konieczny2025	0.06 ± 0.04	0.05 ± 0.05	1.199669	0.144	0.231	0.364
Multimodal	IL5 Konieczny2025	0.08 ± 0.05	0.08 ± 0.05	9441	-0.038	0.717	0.822
Multimodal	IL6 Konieczny2025	0.09 ± 0.06	0.08 ± 0.06	0.725449	0.087	0.469	0.607
Multimodal	IL7 Konieczny2025	-0.02 ± 0.04	-0.03 ± 0.04	2.122498	0.254	0.035	0.079
Multimodal	IL8 Konieczny2025	0.15 ± 0.10	0.13 ± 0.09	1.134974	0.136	0.257	0.391
Multimodal	IL9 Konieczny2025	0.13 ± 0.08	0.11 ± 0.08	2.109252	0.252	0.036	0.082
Multimodal	LDL Graham2021	0.34 ± 0.44	0.26 ± 0.42	1.52056	0.182	0.130	0.231
Multimodal	MDD PGC4 2025	-0.82 ± 0.36	-0.82 ± 0.40	0.01886	0.002	0.985	0.987
Multimodal	MIF Konieczny2025	0.03 ± 0.04	0.04 ± 0.04	-0.25119	-0.030	0.802	0.889
Multimodal	NEUROT DeMoor2015	-0.16 ± 0.05	-0.15 ± 0.05	-1.72294	-0.206	0.086	0.166
Multimodal	OCD PGC3 2018	-0.04 ± 0.32	-0.06 ± 0.33	0.560924	0.067	0.575	0.715
Multimodal	PDGFb Konieczny2025	0.18 ± 0.17	0.18 ± 0.16	0.069341	0.008	0.945	0.963
Multimodal	PTSD Nievergelt2024	-0.31 ± 0.31	-0.35 ± 0.29	1.032314	0.124	0.303	0.442
Multimodal	RANTES Konieczny2025	0.19 ± 0.18	0.17 ± 0.16	10208	0.106	0.437	0.575
Multimodal	SCF Konieczny2025	0.82 ± 0.22	0.85 ± 0.25	-0.91379	-0.109	0.362	0.502
Multimodal	SCGFb Konieczny2025	-0.05 ± 0.24	-0.02 ± 0.27	8944	-0.136	0.271	0.405
Multimodal	SCZ Trubetskoy2022	-5.00 ± 1.07	-5.02 ± 1.22	9799	0.018	0.866	0.928
Multimodal	T2D Verma2024	-12.44 ± 1.16	-12.26 ± 1.22	8758	-0.146	0.168	0.284
Multimodal	TNFa Konieczny2025	0.07 ± 0.04	0.06 ± 0.05	1.602148	0.192	0.110	0.203
Multimodal	TNFb Konieczny2025	0.06 ± 0.05	0.05 ± 0.06	0.463367	0.055	0.643	0.763
Multimodal	TRAIL Konieczny2025	-0.25 ± 0.37	-0.27 ± 0.39	9703	0.043	0.979	0.987
Multimodal	TRIG Graham2021	-1.48 ± 0.40	-1.42 ± 0.37	8436	-0.155	0.063	0.132
Multimodal	VEGF Konieczny2025	-0.56 ± 0.30	-0.58 ± 0.31	0.619919	0.074	0.536	0.679

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C

*motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; DTI, diffusion tensor imaging; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; fMRI, functional magnetic resonance imaging; GM, grey matter; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; rs-fMRI, resting-state fMRI; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; t-fMRI, task-based fMRI; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05*

Table A7. Outcome variable comparisons between clusters resulting from the significant stratification models among the MDD sample of the UKB dataset.

Model	Variable	C10	C11	C12	C13	Statistic	Effect size	p-value	q-value
GM	Death thoughts	0=631; 1=1051	0=735; 1=1135	NA	NA	1.20	0.93	0.274	0.540
	Number of depression episodes	7.60 ± 45.97	6.24 ± 17.79	NA	NA	171409	0.04	0.561	0.811
	Cardiovascular diseases	0=1547; 1=298	0=1742; 1=300	NA	NA	1.59	0.89	0.208	0.540
	Diabetes	0=1784; 1=58	0=2017; 1=23	NA	NA	19.36	0.35	<0.001	<0.001*
	RDS-4	6.03 ± 2.33	6.03 ± 2.27	NA	NA	1696027.5	0.00	0.595	0.811
	PHQ-9	4.32 ± 4.68	4.46 ± 4.72	NA	NA	1797487	-0.03	0.270	0.540
	TRD – history	0=514; 1=32	0=547; 1=31	NA	NA	0.13	0.91	0.717	0.896
	BMI	26.71 ± 4.79	26.78 ± 4.69	NA	NA	1857393.5	-0.02	0.535	0.811
	Ever self-harmed	0=1648; 1=190	0=1820; 1=213	NA	NA	0.02	1.02	0.887	0.918
	Ever attempted suicide	0=81; 1=105	0=105; 1=98	NA	NA	2.60	0.72	0.107	0.540
	Working memory	5.87 ± 1.30	5.95 ± 1.30	NA	NA	703731.5	-0.07	0.192	0.540
	Verbal fluency	21.44 ± 7.60	15.00 ± 8.49	NA	NA	14.00	0.76	0.288	0.540
	Motor speed	573.83 ± 98.99	568.75 ± 95.46	NA	NA	1746067.5	0.05	0.162	0.540
	Processing speed	20.65 ± 5.00	20.74 ± 4.71	NA	NA	669031.5	-0.02	0.910	0.918
	Executive function	10.49 ± 3.22	10.53 ± 3.04	NA	NA	659655.5	-0.01	0.918	0.918
DTI	Death thoughts	0=587; 1=965	0=779; 1=1221	NA	NA	0.47	0.95	0.493	0.663
	Number of depression episodes	5.84 ± 15.57	7.62 ± 42.35	NA	NA	174041	-0.05	0.958	0.958
	Cardiovascular diseases	0=1412; 1=299	0=1877; 1=299	NA	NA	10.26	0.75	0.001	0.007*
	Diabetes	0=1663; 1=46	0=2138; 1=35	NA	NA	5.47	0.59	0.019	0.065
	RDS-4	5.97 ± 2.31	6.07 ± 2.29	NA	NA	1628382	-0.04	0.044	0.089
	PHQ-9	4.29 ± 4.71	4.48 ± 4.69	NA	NA	1744552.5	-0.04	0.042	0.089
	TRD – history	0=487; 1=37	0=574; 1=26	NA	NA	3.93	0.60	0.047	0.089
	BMI	26.59 ± 4.75	26.87 ± 4.73	NA	NA	1777219	-0.06	0.022	0.065
	Ever self-harmed	0=1518; 1=183	0=1950; 1=220	NA	NA	0.39	0.94	0.531	0.663
	Ever attempted suicide	0=87; 1=90	0=99; 1=113	NA	NA	0.23	1.10	0.629	0.726
	Working memory	5.89 ± 1.27	5.93 ± 1.33	NA	NA	701520.5	-0.03	0.360	0.600
	Verbal fluency	17.25 ± 5.91	22.00 ± 8.56	NA	NA	-0.97	-0.56	0.355	0.540
	Motor speed	578.54 ± 100.36	565.35 ± 94.21	NA	NA	1816535.5	0.14	<0.001	<0.001*
	Processing speed	20.33 ± 4.83	20.97 ± 4.84	NA	NA	607133	-0.13	0.001	0.006*
	Executive function	10.51 ± 3.18	10.51 ± 3.08	NA	NA	657117.5	0.00	0.733	0.785
rs-fMRI	Death thoughts	0=275; 1=427	0=422; 1=727	0=364; 1=565	0=305; 1=467	2.17	0.89	0.538	0.733

	Number of depression episodes	5.72 ± 13.20	6.12 ± 19.46	9.97 ± 61.33	5.69 ± 18.32	1.43	0.00	0.698	0.810
	Cardiovascular diseases	0=653; 1=113	0=1044; 1=213	0=853; 1=168	0=739; 1=104	9.50	0.69	0.023	0.117
	Diabetes	0=746; 1=19	0=1223; 1=33	0=999; 1=20	0=833; 1=9	6.73	0.40	0.081	0.303
	RDS-4	6.11 ± 2.29	5.98 ± 2.20	6.09 ± 2.46	5.95 ± 2.25	3.12	0.00	0.373	0.560
	PHQ-9	4.55 ± 4.61	4.25 ± 4.65	4.71 ± 4.98	4.09 ± 4.48	11.07	0.00	0.011	0.085
	TRD – history	0=214; 1=10	0=361; 1=23	0=255; 1=18	0=231; 1=12	1.37	0.66	0.713	0.810
	BMI	27.90 ± 5.15	26.90 ± 4.76	26.71 ± 4.63	25.51 ± 4.13	112.05	0.03	<0.001*	<0.001*
	Ever self-harmed	0=688; 1=75	0=1125; 1=127	0=904; 1=111	0=751; 1=90	0.75	0.89	0.862	0.862
	Ever attempted suicide	0=34; 1=39	0=57; 1=63	0=56; 1=52	0=39; 1=49	1.19	0.74	0.756	0.810
	Working memory	5.89 ± 1.32	5.95 ± 1.36	5.84 ± 1.31	5.99 ± 1.20	4.83	0.00	0.184	0.415
	Verbal fluency	/	17.00 ± 4.85	23.00 ± 3.00	23.00 ± 14.00	0.779	/	0.491	0.733
	Motor speed	572.90 ± 100.44	573.86 ± 97.02	571.83 ± 98.99	564.79 ± 91.94	5.57	0.00	0.134	0.403
	Processing speed	20.60 ± 4.74	20.35 ± 4.96	20.79 ± 4.79	20.97 ± 4.90	4.72	0.00	0.194	0.415
	Executive function	10.38 ± 3.12	10.46 ± 3.16	10.42 ± 3.09	10.79 ± 3.14	4.10	0.00	0.251	0.471
t-fMRI	Death thoughts	0=511; 1=883	0=855; 1=1303	NA	NA	3.14	0.88	0.076	0.191
	Number of depression episodes	5.19 ± 12.14	7.89 ± 41.49	NA	NA	166493.5	-0.08	0.785	0.880
	Cardiovascular diseases	0=1245; 1=269	0=2044; 1=329	NA	NA	10.82	0.74	0.001	0.008*
	Diabetes	0=1478; 1=34	0=2323; 1=47	NA	NA	0.32	0.88	0.572	0.716
	RDS-4	6.13 ± 2.33	5.96 ± 2.28	NA	NA	1708680.5	0.07	0.008	0.033*
	PHQ-9	4.64 ± 4.87	4.24 ± 4.58	NA	NA	1822728	0.08	0.024	0.071
	TRD – history	0=448; 1=31	0=613; 1=32	NA	NA	1.19	0.75	0.276	0.414
	BMI	27.00 ± 4.90	26.59 ± 4.63	NA	NA	1881471.5	0.09	0.009	0.033*
	Ever self-harmed	0=1354; 1=155	0=2114; 1=248	NA	NA	0.05	1.02	0.821	0.880
	Ever attempted suicide	0=65; 1=86	0=121; 1=117	NA	NA	2.25	0.73	0.134	0.286
	Working memory	5.89 ± 1.35	5.93 ± 1.26	NA	NA	706485.5	-0.03	0.907	0.907
	Verbal fluency	18.20 ± 6.46	22.00 ± 8.90	NA	NA	-0.79	-0.44	0.447	0.611
	Motor speed	573.94 ± 99.82	569.41 ± 95.44	NA	NA	1663383	0.05	0.171	0.320
	Processing speed	20.31 ± 4.81	20.97 ± 4.85	NA	NA	594829	-0.14	<0.001	0.004*
	Executive function	10.43 ± 3.13	10.57 ± 3.12	NA	NA	625608.5	-0.05	0.250	0.414
PGSs	Death thoughts	0=687; 1=1084	0=679; 1=1102	NA	NA	0.17	1.03	0.683	0.917
	Number of depression episodes	6.08 ± 18.11	7.63 ± 43.85	NA	NA	180340	-0.05	0.562	0.843
	Cardiovascular diseases	0=1636; 1=309	0=1653; 1=289	NA	NA	0.75	0.93	0.385	0.843

	Diabetes	0=1898; 1=46	0=1903; 1=35	NA	NA	1.49	0.76	0.222	0.843
	RDS-4	6.03 ± 2.32	6.03 ± 2.28	NA	NA	1719245	0.00	0.939	0.995
	PHQ-9	4.41 ± 4.78	4.38 ± 4.62	NA	NA	1830643	0.01	0.777	0.917
	TRD – history	0=532; 1=37	0=529; 1=26	NA	NA	1.76	0.71	0.185	0.843
	BMI	26.80 ± 4.75	26.69 ± 4.74	NA	NA	1919617.5	0.02	0.304	0.843
	Ever self-harmed	0=1723; 1=213	0=1745; 1=190	NA	NA	1.45	0.88	0.228	0.843
	Ever attempted suicide	0=93; 1=109	0=93; 1=94	NA	NA	0.53	0.86	0.466	0.843
	Working memory	5.91 ± 1.35	5.92 ± 1.25	NA	NA	730316	-0.01	0.995	0.995
	Verbal fluency	17.50 ± 6.28	23.60 ± 8.71	NA	NA	8.50	-0.75	0.272	0.843
	Motor speed	571.09 ± 98.17	571.25 ± 96.19	NA	NA	1696331.5	0.00	0.795	0.917
	Processing speed	20.71 ± 4.99	20.69 ± 4.69	NA	NA	685088	0.00	0.561	0.843
	Executive function	10.44 ± 3.13	10.57 ± 3.13	NA	NA	655517	-0.04	0.494	0.843
	Multimodal								
	Death thoughts	0=737; 1=1131	0=629; 1=1055	NA	NA	1.65	1.09	0.198	0.319
	Number of depression episodes	7.66 ± 43.56	5.93 ± 15.56	NA	NA	173256	0.05	0.572	0.780
	Cardiovascular diseases	0=1755; 1=275	0=1534; 1=323	NA	NA	11.02	1.34	0.001	0.013*
	Diabetes	0=1997; 1=30	0=1804; 1=51	NA	NA	7.64	1.88	0.006	0.021*
	RDS-4	6.05 ± 2.27	6.00 ± 2.32	NA	NA	1755751	0.02	0.187	0.319
	PHQ-9	4.54 ± 4.67	4.24 ± 4.73	NA	NA	1941023	0.06	0.002	0.015*
	TRD – history	0=548; 1=26	0=513; 1=37	NA	NA	2.56	1.52	0.109	0.273
	BMI	26.85 ± 4.73	26.64 ± 4.75	NA	NA	1933093	0.04	0.128	0.274
	Ever self-harmed	0=1816; 1=209	0=1652; 1=194	NA	NA	0.04	1.02	0.848	0.856
	Ever attempted suicide	0=97; 1=104	0=89; 1=99	NA	NA	0.03	1.04	0.856	0.856
	Working memory	5.95 ± 1.30	5.87 ± 1.30	NA	NA	747103	0.06	0.212	0.319
	Verbal fluency	20.00 ± 6.52	20.50 ± 9.29	NA	NA	-0.10	-0.06	0.922	0.922
	Motor speed	566.95 ± 95.45	575.76 ± 98.85	NA	NA	1605457.5	-0.09	0.003	0.015*
	Processing speed	20.93 ± 4.88	20.42 ± 4.79	NA	NA	713138	0.11	0.010	0.030*
	Executive function	10.48 ± 3.07	10.54 ± 3.19	NA	NA	655986	-0.02	0.698	0.856

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; CI, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; NA, not applicable; NA, not applicable; PGSs, polygenic scores; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Table A8. Outcome variable comparisons between clusters resulting from the significant stratification models among the dMDD sample of the UKB dataset.

Model	Variable	CI0	CI1	Statistic	Effect size	p-value	q-value
GM	Death thoughts	0=29; 1=96	0=35; 1=97	0.38	0.837	0.539	0.755
	Number of depression episodes	27.88 ± 61.73	12.19 ± 19.72	592.00	0.345	0.986	0.986
	Cardiovascular diseases	0=109; 1=27	0=109; 1=34	0.63	1.259	0.428	0.666
	Diabetes	0=132; 1=3	0=133; 1=10	3.55	3.308	0.060	0.279
	RDS-4	12.02 ± 2.01	11.80 ± 1.88	10251.50	0.115	0.422	0.666
	PHQ-9	11.46 ± 6.55	11.50 ± 6.34	9281.50	-0.006	0.958	0.986
	TRD – history	0=44; 1=9	0=44; 1=10	0.04	1.111	0.835	0.986
	BMI	28.07 ± 5.73	28.09 ± 6.01	9764.50	-0.003	0.953	0.986
	Ever self-harmed	0=110; 1=25	0=109; 1=32	0.73	1.292	0.392	0.666
	Ever attempted suicide	0=14; 1=10	0=12; 1=20	2.39	2.333	0.122	0.341
	Working memory	6.01 ± 1.33	5.81 ± 1.56	3793.50	0.137	0.383	0.666
	Motor speed	563.95 ± 92.10	596.01 ± 119.23	7480.50	-0.299	0.030	0.212
	Processing speed	21.51 ± 4.64	19.49 ± 6.00	4004.50	0.375	0.015	0.211
	Executive function	10.62 ± 3.24	9.76 ± 3.18	1.70	0.267	0.091	0.319
DTI	Death thoughts	0=25; 1=90	0=39; 1=103	1.11	0.734	0.291	0.807
	Number of depression episodes	13.89 ± 15.84	23.66 ± 57.32	706.50	-0.213	0.105	0.734
	Cardiovascular diseases	0=101; 1=24	0=117; 1=37	0.94	1.331	0.332	0.807
	Diabetes	0=120; 1=5	0=145; 1=8	0.23	1.324	0.629	0.812
	RDS-4	11.91 ± 1.92	11.90 ± 1.97	9722.50	0.005	0.882	0.950
	PHQ-9	11.72 ± 6.48	11.30 ± 6.40	9501.00	0.065	0.638	0.812
	TRD – history	0=42; 1=9	0=46; 1=10	0.00	1.014	0.977	0.977
	BMI	27.84 ± 5.67	28.28 ± 6.04	9296.00	-0.074	0.624	0.812
	Ever self-harmed	0=97; 1=26	0=122; 1=31	0.03	0.948	0.858	0.950
	Ever attempted suicide	0=11; 1=15	0=15; 1=15	0.33	0.733	0.565	0.812
	Working memory	5.75 ± 1.35	6.03 ± 1.52	3182.50	-0.191	0.346	0.807
	Motor speed	586.22 ± 113.04	575.52 ± 103.51	9264.00	0.099	0.420	0.812
	Processing speed	19.64 ± 5.19	21.13 ± 5.58	-1.73	-0.273	0.085	0.734
	Executive function	9.80 ± 3.26	10.49 ± 3.19	-1.36	-0.216	0.177	0.807
rs-fMRI	Death thoughts	0=31; 1=81	0=33; 1=112	0.82	1.299	0.366	0.512
	Number of depression episodes	12.35 ± 27.54	26.83 ± 57.17	422.00	-0.318	0.037	0.174
	Cardiovascular diseases	0=101; 1=21	0=117; 1=40	2.74	1.644	0.098	0.273
	Diabetes	0=112; 1=9	0=153; 1=4	3.67	0.325	0.056	0.194
	RDS-4	11.66 ± 1.95	12.10 ± 1.92	8187.00	-0.222	0.033	0.174
	PHQ-9	10.44 ± 6.03	12.29 ± 6.63	7647.00	-0.290	0.019	0.174
	TRD – history	0=38; 1=5	0=50; 1=14	1.85	2.128	0.174	0.406
	BMI	27.79 ± 5.58	28.30 ± 6.09	9104.00	-0.087	0.480	0.611
	Ever self-harmed	0=100; 1=21	0=119; 1=36	1.43	1.441	0.232	0.433
	Ever attempted suicide	0=9; 1=12	0=17; 1=18	0.17	0.794	0.678	0.730
	Working memory	5.90 ± 1.29	5.91 ± 1.54	3351.50	-0.006	0.883	0.883
	Motor speed	589.97 ± 110.26	573.12 ± 105.78	9383.00	0.156	0.247	0.433

	Processing speed	21.10 ± 5.00	20.14 ± 5.68	1.09	0.176	0.279	0.434
	Executive function	10.37 ± 2.90	10.09 ± 3.41	0.54	0.087	0.593	0.692
t-fMRI	Death thoughts	0=19; 1=63	0=45; 1=130	0.19	0.871	0.660	0.840
	Number of depression episodes	6.00 ± 5.61	28.50 ± 56.45	467.50	-0.502	0.221	0.773
	Cardiovascular diseases	0=71; 1=19	0=147; 1=42	0.04	1.068	0.834	0.898
	Diabetes	0=85; 1=5	0=180; 1=8	NA	0.756	0.762	0.889
	RDS-4	11.57 ± 1.90	12.07 ± 1.95	7173.00	-0.259	0.030	0.254
	PHQ-9	11.70 ± 6.04	11.38 ± 6.62	8368.00	0.049	0.649	0.840
	TRD – history	0=27; 1=10	0=61; 1=9	3.33	0.398	0.068	0.318
	BMI	29.07 ± 5.85	27.61 ± 5.83	9825.00	0.250	0.036	0.254
	Ever self-harmed	0=68; 1=21	0=151; 1=36	0.69	0.772	0.405	0.840
	Ever attempted suicide	0=11; 1=10	0=15; 1=20	0.48	1.467	0.489	0.840
	Working memory	5.98 ± 1.85	5.88 ± 1.24	3158.00	0.069	0.615	0.840
	Motor speed	579.64 ± 115.09	580.69 ± 104.47	7716.00	-0.010	0.905	0.905
	Processing speed	19.96 ± 5.03	20.72 ± 5.63	-0.82	-0.139	0.412	0.840
	Executive function	10.00 ± 3.38	10.28 ± 3.17	2524.00	-0.086	0.468	0.840
PGSs	Death thoughts	0=34; 1=87	0=30; 1=106	1.25	1.381	0.264	0.587
	Number of depression episodes	24.30 ± 60.01	15.47 ± 25.73	638.00	0.192	0.599	0.699
	Cardiovascular diseases	0=100; 1=27	0=118; 1=34	0.05	1.067	0.823	0.823
	Diabetes	0=122; 1=5	0=143; 1=8	0.29	1.365	0.592	0.699
	RDS-4	12.24 ± 2.07	11.62 ± 1.79	11268.00	0.321	0.013	0.094
	PHQ-9	12.70 ± 6.66	10.45 ± 6.07	11066.50	0.354	0.005	0.072
	TRD – history	0=47; 1=8	0=41; 1=11	0.80	1.576	0.371	0.587
	BMI	28.85 ± 6.30	27.44 ± 5.42	11118.50	0.242	0.029	0.135
	Ever self-harmed	0=96; 1=30	0=123; 1=27	1.41	0.702	0.235	0.587
	Ever attempted suicide	0=15; 1=14	0=11; 1=16	0.68	1.558	0.410	0.587
	Working memory	5.85 ± 1.60	5.96 ± 1.34	3223.50	0.074	0.420	0.587
	Motor speed	585.41 ± 98.18	576.18 ± 115.34	9573.00	0.085	0.193	0.587
	Processing speed	20.00 ± 5.64	20.87 ± 5.30	-1.01	-0.159	0.316	0.587
	Executive function	10.10 ± 3.42	10.26 ± 3.09	-0.31	-0.050	0.754	0.812
Multimodal	Death thoughts	0=29; 1=94	0=35; 1=99	0.22	0.873	0.638	0.865
	Number of depression episodes	11.55 ± 13.50	26.34 ± 59.40	686.50	-0.325	0.239	0.670
	Cardiovascular diseases	0=103; 1=27	0=115; 1=34	0.17	1.128	0.679	0.865
	Diabetes	0=121; 1=9	0=144; 1=4	2.77	0.373	0.096	0.449
	RDS-4	11.85 ± 1.88	11.95 ± 2.00	9560.00	-0.051	0.849	0.866
	PHQ-9	11.94 ± 6.58	11.10 ± 6.29	9940.00	0.130	0.296	0.691
	TRD – history	0=39; 1=9	0=49; 1=10	0.06	0.884	0.808	0.866
	BMI	28.15 ± 5.53	28.02 ± 6.16	10143.50	0.022	0.496	0.771
	Ever self-harmed	0=101; 1=27	0=118; 1=30	0.03	0.951	0.866	0.866
	Ever attempted suicide	0=11; 1=16	0=15; 1=14	0.68	0.642	0.410	0.718
	Working memory	5.81 ± 1.57	5.99 ± 1.35	3209.50	-0.012	0.359	0.718
	Motor speed	591.56 ± 115.29	570.26 ± 100.01	9914.00	0.198	0.081	0.449
	Processing speed	19.49 ± 5.00	21.26 ± 5.68	-2.07	-0.327	0.040	0.449

	Executive function	9.83 ± 3.06	10.47 ± 3.34	-1.26	-0.200	0.211	0.670

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; CI, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; PHQ-9, Patient Health Questionnaire-9; RDS-4, Recent Depressive Symptoms; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI; TRD, treatment-resistant depression.

*Statistical significance at FDR-corrected p -value (i.e., q -value) < 0.05

Table A9. Outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD sample of the UKB dataset.

Model	Variable	Cluster	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	Diabetes	C10	0.577	58.78	62.07	55.49	0.012	0.036*
	Diabetes	C11	0.581	55.44	52.17	58.70	0.172	0.258
	Ever attempted suicide	C11	0.470	46.29	45.92	46.67	0.782	0.792
	Ever self-harmed	C10	0.491	50.92	54.21	47.63	0.309	0.397
	Ever self-harmed	C11	0.473	48.24	45.54	50.93	0.792	0.792
	Cardiovascular diseases	C10	0.566	55.26	55.70	54.82	0.003	0.013*
	Cardiovascular diseases	C11	0.568	55.00	53.33	56.66	0.002	0.013*
	TRD – history	C10	0.524	55.28	62.50	48.05	0.148	0.258
	TRD – history	C11	0.573	55.76	54.84	56.67	0.145	0.258
DTI	Diabetes	C10	0.542	54.68	54.35	55.02	0.139	0.312
	Diabetes	C11	0.662	63.89	62.86	64.92	0.001	0.004*
	Ever attempted suicide	C10	0.538	51.49	46.67	56.32	0.349	0.451
	Ever self-harmed	C10	0.528	51.51	49.73	53.29	0.261	0.451
	Ever self-harmed	C11	0.525	50.73	48.64	52.82	0.351	0.451
	Cardiovascular diseases	C10	0.617	58.83	57.53	60.13	0.001	0.004*
	Cardiovascular diseases	C11	0.582	54.87	53.85	55.89	0.004	0.012*
	TRD – history	C10	0.472	49.99	48.65	51.33	0.496	0.557
	TRD – history	C11	0.512	47.99	46.15	49.83	0.614	0.614
rs-fMRI	Diabetes	C10	0.612	58.22	52.63	63.81	0.118	0.501
	Diabetes	C11	0.533	50.57	48.48	52.66	0.422	0.796
	Diabetes	C12	0.620	65.93	75.00	56.86	0.005	0.042*
	Diabetes	C13	0.546	50.07	44.44	55.70	0.477	0.810
	Ever attempted suicide	C10	0.559	55.05	51.28	58.82	0.221	0.556
	Ever self-harmed	C10	0.556	51.74	53.33	50.15	0.307	0.652
	Ever self-harmed	C11	0.445	45.53	41.73	49.33	0.948	0.948
	Ever self-harmed	C12	0.464	47.14	45.95	48.34	0.833	0.891
	Ever self-harmed	C13	0.474	48.17	50.00	46.34	0.690	0.891
	Cardiovascular diseases	C10	0.630	60.53	61.95	59.11	0.001	0.017*
	Cardiovascular diseases	C11	0.573	54.69	53.05	56.32	0.021	0.119
	Cardiovascular diseases	C12	0.523	49.88	45.83	53.93	0.548	0.848
	Cardiovascular diseases	C13	0.518	52.14	50.96	53.32	0.229	0.556
	TRD – history	C10	0.380	43.93	50.00	37.85	0.773	0.891
	TRD – history	C11	0.579	56.10	56.52	55.68	0.165	0.556
	TRD – history	C12	0.484	47.97	55.56	40.39	0.599	0.849
	TRD – history	C13	0.431	41.77	33.33	50.22	0.838	0.891
t-fMRI	Diabetes	C10	0.418	42.63	38.24	47.02	0.940	0.955
	Diabetes	C11	0.472	47.32	46.81	47.83	0.743	0.955
	Ever attempted suicide	C10	0.496	52.66	40.70	64.62	0.313	0.730
	Ever self-harmed	C10	0.526	52.49	50.32	54.65	0.169	0.591
	Ever self-harmed	C11	0.509	50.15	54.03	46.26	0.472	0.825
	Cardiovascular diseases	C10	0.507	51.92	54.28	49.56	0.152	0.591

	Cardiovascular diseases	CII	0.472	47.09	44.38	49.80	0.955	0.955
PGSs	Diabetes	CI0	0.639	60.34	63.04	57.64	0.011	0.088
	Diabetes	CII	0.463	50.12	42.86	57.38	0.511	0.585
	Ever self-harmed	CI0	0.548	52.26	51.17	53.34	0.135	0.353
	Ever self-harmed	CII	0.540	51.91	53.16	50.66	0.221	0.353
	Cardiovascular diseases	CI0	0.539	51.51	51.13	51.89	0.190	0.353
	Cardiovascular diseases	CII	0.542	52.41	52.25	52.57	0.090	0.353
	TRD – history	CI0	0.537	52.34	56.76	47.93	0.337	0.449
	TRD – history	CII	0.458	44.78	42.31	47.26	0.854	0.854
Multimodal	Diabetes	CI0	0.674	63.25	66.67	59.84	0.004	0.012*
	Diabetes	CII	0.606	58.42	56.86	59.98	0.021	0.047*
	Ever attempted suicide	CI0	0.516	53.18	54.81	51.55	0.225	0.337
	Ever self-harmed	CI0	0.527	51.68	52.15	51.21	0.209	0.337
	Ever self-harmed	CII	0.480	46.79	43.81	49.76	0.930	0.930
	Cardiovascular diseases	CI0	0.580	55.45	54.55	56.35	0.002	0.009*
	Cardiovascular diseases	CII	0.637	59.58	60.68	58.47	0.001	0.009*
	TRD – history	CI0	0.498	49.36	50.00	48.72	0.550	0.619
	TRD – history	CII	0.517	53.05	54.05	52.05	0.268	0.344

*N.B. Missing models were not computed due to insufficient cases in the corresponding cluster. Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; CI, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) < 0.05*

Table A10. Outcome variables' predictions within each cluster resulting from the significant stratification models among the dMDD sample of the UKB dataset.

Model	Variable	Cluster	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
GM	Diabetes	C11	0.761	72.33	80.00	64.66	0.008	0.056
	Ever self-harmed	C10	0.448	44.00	48.00	40.00	0.842	0.842
	Ever self-harmed	C11	0.529	48.29	40.63	55.96	0.599	0.839
	Cardiovascular diseases	C10	0.502	53.01	55.56	50.46	0.336	0.783
	Cardiovascular diseases	C11	0.487	46.74	41.18	52.29	0.734	0.842
	TRD – history	C10	0.434	49.49	44.44	54.55	0.482	0.839
	TRD – history	C11	0.659	63.41	70.00	56.82	0.110	0.385
DTI	Ever self-harmed	C10	0.546	55.79	53.85	57.73	0.217	0.434
	Ever self-harmed	C11	0.493	50.78	54.84	46.72	0.438	0.700
	Thoughts of death during worst depression	C10	0.452	39.67	43.33	36.00	0.939	0.939
	Thoughts of death during worst depression	C11	0.476	43.64	43.69	43.59	0.879	0.939
	Cardiovascular diseases	C10	0.434	42.72	45.83	39.60	0.871	0.939
	Cardiovascular diseases	C11	0.656	62.42	67.57	57.26	0.012	0.056
	TRD – history	C10	0.624	58.73	55.56	61.90	0.198	0.434
rs-fMRI	TRD – history	C11	0.604	72.61	80.00	65.22	0.014	0.056
	Diabetes	C10	0.400	41.67	33.33	50.00	0.810	0.810
	Ever attempted suicide	C10	0.593	56.94	58.33	55.56	0.312	0.501
	Ever self-harmed	C10	0.562	54.19	52.38	56.00	0.272	0.501
	Ever self-harmed	C11	0.501	46.85	50.00	43.70	0.708	0.810
	Cardiovascular diseases	C10	0.587	58.49	71.43	45.54	0.114	0.501
	Cardiovascular diseases	C11	0.585	54.00	55.00	52.99	0.250	0.501
t-fMRI	TRD – history	C11	0.494	53.57	57.14	50.00	0.358	0.501
	Diabetes	C11	0.511	49.31	37.50	61.11	0.565	0.695
	Ever attempted suicide	C11	0.413	46.67	40.00	53.33	0.703	0.703
	Ever self-harmed	C10	0.673	66.25	61.90	70.59	0.011	0.035*
	Ever self-harmed	C11	0.623	62.21	69.44	54.97	0.013	0.035*
	Cardiovascular diseases	C10	0.599	60.97	68.42	53.52	0.067	0.134
	Cardiovascular diseases	C11	0.562	52.89	54.76	51.02	0.300	0.480
PGSs	TRD – history	C10	0.715	74.63	90.00	59.26	0.009	0.035*
	TRD – history	C11	0.579	48.27	55.56	40.98	0.608	0.695
	Diabetes	C11	0.556	54.02	50.00	58.04	0.309	0.823
	Ever attempted suicide	C11	0.545	44.60	43.75	45.45	0.720	0.922
	Ever self-harmed	C10	0.561	55.83	53.33	58.33	0.183	0.731
	Ever self-harmed	C11	0.419	42.10	37.04	47.15	0.922	0.922
	Cardiovascular diseases	C10	0.567	56.63	59.26	54.00	0.156	0.731
Multimodal	Cardiovascular diseases	C11	0.479	45.81	38.24	53.39	0.757	0.922
	TRD – history	C10	0.253	39.10	25.00	53.19	0.843	0.922
	TRD – history	C11	0.377	41.02	45.45	36.59	0.819	0.922
	Diabetes	C10	0.718	63.91	66.67	61.16	0.078	0.273
	Ever attempted suicide	C10	0.563	52.27	50.00	54.55	0.456	0.784

	Ever self-harmed	CI0	0.453	48.09	40.74	55.45	0.572	0.784
	Ever self-harmed	CI1	0.490	45.79	46.67	44.92	0.767	0.784
	Cardiovascular diseases	CI0	0.504	51.26	48.15	54.37	0.396	0.784
	Cardiovascular diseases	CI1	0.623	58.81	55.88	61.74	0.066	0.273
	TRD – history	CI1	0.349	42.55	30.00	55.10	0.784	0.784

*N.B. Missing models were not computed due to insufficient cases in the corresponding cluster. Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; CI, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; GM, grey matter; PGSs, polygenic scores; rs-fMRI, resting-state fMRI; t-fMRI, task-based fMRI; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05*

Table A11. Bootstrap results of the elastic-net penalized regression model predicting diabetes within C10 of the multimodal stratification among the MDD sample of the UKB dataset.

Variable	Mean	SD	LowerCI	UpperCI	VIP	Significance
Area of caudalanteriorcingulate L	-0.023	0.013	-0.049	0.003	100	No
Area of caudalanteriorcingulate R	-0.010	0.013	-0.037	0.014	100	No
Area of caudalmiddlefrontal L	-0.009	0.011	-0.031	0.011	100	No
Area of caudalmiddlefrontal R	-0.009	0.012	-0.035	0.014	100	No
Area of cuneus L	-0.009	0.011	-0.031	0.013	100	No
Area of cuneus R	-0.011	0.011	-0.033	0.011	100	No
Area of entorhinal L	0.011	0.014	-0.016	0.039	100	No
Area of entorhinal R	0.014	0.013	-0.013	0.040	100	No
Area of fusiform L	0.019	0.013	-0.008	0.045	100	No
Area of fusiform R	0.005	0.014	-0.022	0.032	100	No
Area of inferiorparietal L	-0.013	0.014	-0.040	0.017	100	No
Area of inferiorparietal R	-0.011	0.013	-0.037	0.012	100	No
Area of inferiortemporal L	0.012	0.013	-0.011	0.039	100	No
Area of inferiortemporal R	-0.003	0.013	-0.028	0.021	100	No
Area of insula L	0.008	0.012	-0.016	0.032	100	No
Area of insula R	0.015	0.013	-0.010	0.037	100	No
Area of isthmuscingulate L	0.003	0.014	-0.027	0.031	100	No
Area of isthmuscingulate R	-0.001	0.013	-0.026	0.023	100	No
Area of lateraloccipital L	0.003	0.012	-0.020	0.026	100	No
Area of lateraloccipital R	0.006	0.014	-0.022	0.034	100	No
Area of lateralorbitofrontal L	0.005	0.011	-0.017	0.028	100	No
Area of lateralorbitofrontal R	0.004	0.012	-0.020	0.028	100	No
Area of lingual L	0.007	0.011	-0.015	0.028	100	No
Area of lingual R	0.011	0.012	-0.012	0.036	100	No
Area of medialorbitofrontal L	0.001	0.013	-0.023	0.025	100	No
Area of medialorbitofrontal R	-0.003	0.013	-0.028	0.023	100	No
Area of middletemporal L	0.013	0.013	-0.011	0.039	100	No
Area of middletemporal R	-0.002	0.011	-0.022	0.020	100	No
Area of paracentral L	0.003	0.012	-0.022	0.026	100	No
Area of paracentral R	-0.007	0.012	-0.031	0.016	100	No
Area of parahippocampal L	0.005	0.013	-0.019	0.029	100	No
Area of parahippocampal R	0.005	0.014	-0.023	0.033	100	No
Area of parsopercularis L	0.010	0.012	-0.014	0.034	100	No
Area of parsopercularis R	0.002	0.013	-0.022	0.028	100	No
Area of parsorbitalis L	0.011	0.013	-0.014	0.036	100	No
Area of parsorbitalis R	0.006	0.013	-0.019	0.030	100	No
Area of parstriangularis L	0.005	0.013	-0.021	0.030	100	No
Area of parstriangularis R	0.006	0.013	-0.020	0.031	100	No
Area of pericalcarine L	-0.006	0.011	-0.028	0.016	100	No
Area of pericalcarine R	-0.004	0.011	-0.026	0.018	100	No
Area of postcentral L	-0.014	0.013	-0.039	0.010	100	No

Area of postcentral R	0.002	0.012	-0.020	0.025	100	No
Area of posteriorcingulate L	-0.021	0.012	-0.046	0.003	100	No
Area of posteriorcingulate R	-0.008	0.013	-0.034	0.017	100	No
Area of precentral L	-0.005	0.012	-0.029	0.019	100	No
Area of precentral R	-0.002	0.012	-0.024	0.021	100	No
Area of precuneus L	-0.006	0.012	-0.030	0.017	100	No
Area of precuneus R	-0.001	0.010	-0.020	0.020	100	No
Area of rostralanteriorcingulate L	-0.005	0.013	-0.032	0.021	100	No
Area of rostralanteriorcingulate R	0.001	0.012	-0.022	0.024	100	No
Area of rostralmiddlefrontal L	-0.009	0.011	-0.032	0.013	100	No
Area of rostralmiddlefrontal R	-0.001	0.012	-0.024	0.022	100	No
Area of superiorfrontal L	0.000	0.011	-0.022	0.021	100	No
Area of superiorfrontal R	-0.003	0.013	-0.027	0.024	100	No
Area of superiorparietal L	0.003	0.011	-0.019	0.027	100	No
Area of superiorparietal R	0.004	0.013	-0.023	0.030	100	No
Area of superiortemporal L	-0.001	0.013	-0.026	0.024	100	No
Area of superiortemporal R	0.005	0.012	-0.019	0.029	100	No
Area of supramarginal L	-0.003	0.013	-0.027	0.021	100	No
Area of supramarginal R	0.001	0.012	-0.021	0.024	100	No
Area of transversetemporal L	0.008	0.013	-0.018	0.034	100	No
Area of transversetemporal R	0.002	0.013	-0.024	0.027	100	No
Mean thickness of caudalanteriorcingulate L	0.004	0.013	-0.021	0.030	100	No
Mean thickness of caudalanteriorcingulate R	0.000	0.013	-0.025	0.027	100	No
Mean thickness of caudalmiddlefrontal L	-0.001	0.011	-0.021	0.020	100	No
Mean thickness of caudalmiddlefrontal R	-0.009	0.011	-0.029	0.012	100	No
Mean thickness of cuneus L	0.008	0.011	-0.015	0.030	100	No
Mean thickness of cuneus R	0.020	0.012	-0.001	0.042	100	No
Mean thickness of entorhinal L	-0.008	0.015	-0.036	0.023	100	No
Mean thickness of entorhinal R	-0.002	0.013	-0.025	0.024	100	No
Mean thickness of fusiform L	-0.009	0.012	-0.031	0.015	100	No
Mean thickness of fusiform R	-0.011	0.012	-0.034	0.013	100	No
Mean thickness of inferiorparietal L	-0.009	0.011	-0.030	0.011	100	No
Mean thickness of inferiorparietal R	-0.013	0.012	-0.036	0.009	100	No
Mean thickness of inferiortemporal L	-0.005	0.012	-0.028	0.019	100	No
Mean thickness of inferiortemporal R	-0.008	0.012	-0.033	0.017	100	No
Mean thickness of insula L	-0.006	0.013	-0.030	0.022	100	No
Mean thickness of insula R	-0.030	0.012	-0.054	-0.008	100	Yes*
Mean thickness of isthmuscingulate L	0.012	0.013	-0.014	0.037	100	No
Mean thickness of isthmuscingulate R	0.000	0.014	-0.025	0.028	100	No
Mean thickness of lateraloccipital L	-0.006	0.012	-0.027	0.018	100	No
Mean thickness of lateraloccipital R	-0.007	0.011	-0.028	0.014	100	No
Mean thickness of lateralorbitofrontal L	-0.014	0.012	-0.036	0.009	100	No
Mean thickness of lateralorbitofrontal R	-0.012	0.013	-0.038	0.012	100	No
Mean thickness of lingual L	0.004	0.012	-0.018	0.028	100	No

Mean thickness of lingual R	0.009	0.012	-0.014	0.033	100	No
Mean thickness of medialorbitofrontal L	0.004	0.013	-0.022	0.030	100	No
Mean thickness of medialorbitofrontal R	0.003	0.014	-0.024	0.028	100	No
Mean thickness of middletemporal L	-0.008	0.012	-0.030	0.015	100	No
Mean thickness of middletemporal R	-0.006	0.012	-0.029	0.018	100	No
Mean thickness of paracentral L	-0.010	0.012	-0.033	0.014	100	No
Mean thickness of paracentral R	-0.014	0.012	-0.037	0.007	100	No
Mean thickness of parahippocampal L	0.000	0.013	-0.024	0.024	100	No
Mean thickness of parahippocampal R	-0.008	0.014	-0.035	0.022	100	No
Mean thickness of parsopercularis L	-0.006	0.012	-0.029	0.018	100	No
Mean thickness of parsopercularis R	-0.007	0.012	-0.029	0.020	100	No
Mean thickness of parsorbitalis L	0.006	0.013	-0.019	0.031	100	No
Mean thickness of parsorbitalis R	0.002	0.013	-0.024	0.028	100	No
Mean thickness of parstriangularis L	0.003	0.012	-0.020	0.026	100	No
Mean thickness of parstriangularis R	-0.018	0.012	-0.043	0.007	100	No
Mean thickness of pericalcarine L	0.019	0.013	-0.005	0.043	100	No
Mean thickness of pericalcarine R	0.007	0.012	-0.018	0.031	100	No
Mean thickness of postcentral L	-0.009	0.011	-0.029	0.013	100	No
Mean thickness of postcentral R	-0.007	0.010	-0.027	0.012	100	No
Mean thickness of posteriorcingulate L	0.003	0.013	-0.020	0.028	100	No
Mean thickness of posteriorcingulate R	-0.012	0.015	-0.040	0.017	100	No
Mean thickness of precentral L	-0.005	0.011	-0.027	0.016	100	No
Mean thickness of precentral R	-0.003	0.011	-0.023	0.020	100	No
Mean thickness of precuneus L	0.000	0.012	-0.022	0.022	100	No
Mean thickness of precuneus R	-0.010	0.011	-0.033	0.012	100	No
Mean thickness of rostralanteriorcingulate L	0.007	0.013	-0.018	0.033	100	No
Mean thickness of rostralanteriorcingulate R	-0.010	0.014	-0.036	0.016	100	No
Mean thickness of rostralmiddlefrontal L	-0.001	0.011	-0.022	0.020	100	No
Mean thickness of rostralmiddlefrontal R	-0.001	0.011	-0.021	0.019	100	No
Mean thickness of superiorfrontal L	-0.004	0.010	-0.024	0.016	100	No
Mean thickness of superiorfrontal R	-0.005	0.010	-0.027	0.015	100	No
Mean thickness of superiorparietal L	0.003	0.010	-0.016	0.024	100	No
Mean thickness of superiorparietal R	-0.005	0.011	-0.026	0.017	100	No
Mean thickness of superiortemporal L	0.010	0.011	-0.011	0.032	100	No
Mean thickness of superiortemporal R	-0.004	0.011	-0.026	0.019	100	No
Mean thickness of supramarginal L	0.003	0.010	-0.016	0.023	100	No
Mean thickness of supramarginal R	-0.014	0.011	-0.036	0.008	100	No
Mean thickness of transversetemporal L	-0.021	0.013	-0.046	0.005	100	No
Mean thickness of transversetemporal R	-0.007	0.013	-0.033	0.019	100	No
Volume of caudalanteriorcingulate L	-0.018	0.012	-0.043	0.006	100	No
Volume of caudalanteriorcingulate R	-0.011	0.013	-0.037	0.014	100	No
Volume of caudalmiddlefrontal L	-0.007	0.011	-0.028	0.015	100	No
Volume of caudalmiddlefrontal R	-0.011	0.013	-0.036	0.012	100	No
Volume of cuneus L	-0.003	0.012	-0.027	0.020	100	No

Volume of cuneus R	0.003	0.012	-0.020	0.026	100	No
Volume of entorhinal L	-0.001	0.014	-0.028	0.025	100	No
Volume of entorhinal R	0.007	0.014	-0.022	0.033	100	No
Volume of fusiform L	0.012	0.013	-0.013	0.036	100	No
Volume of fusiform R	0.001	0.013	-0.026	0.026	100	No
Volume of inferiorparietal L	-0.016	0.014	-0.045	0.012	100	No
Volume of inferiorparietal R	-0.017	0.012	-0.040	0.005	100	No
Volume of inferiortemporal L	0.005	0.013	-0.020	0.030	100	No
Volume of inferiortemporal R	-0.006	0.013	-0.032	0.019	100	No
Volume of insula L	-0.001	0.012	-0.024	0.022	100	No
Volume of insula R	-0.007	0.012	-0.031	0.015	100	No
Volume of isthmuscingulate L	0.004	0.014	-0.022	0.032	100	No
Volume of isthmuscingulate R	-0.004	0.013	-0.029	0.022	100	No
Volume of lateraloccipital L	-0.001	0.012	-0.024	0.022	100	No
Volume of lateraloccipital R	-0.001	0.013	-0.029	0.025	100	No
Volume of lateralorbitofrontal L	-0.012	0.012	-0.037	0.011	100	No
Volume of lateralorbitofrontal R	-0.012	0.012	-0.035	0.013	100	No
Volume of lingual L	0.009	0.012	-0.015	0.033	100	No
Volume of lingual R	0.015	0.012	-0.010	0.040	100	No
Volume of medialorbitofrontal L	-0.002	0.013	-0.027	0.022	100	No
Volume of medialorbitofrontal R	0.003	0.013	-0.023	0.029	100	No
Volume of middletemporal L	0.009	0.014	-0.018	0.037	100	No
Volume of middletemporal R	-0.005	0.012	-0.028	0.017	100	No
Volume of paracentral L	-0.006	0.013	-0.032	0.019	100	No
Volume of paracentral R	-0.017	0.011	-0.038	0.005	100	No
Volume of parahippocampal L	0.005	0.013	-0.020	0.031	100	No
Volume of parahippocampal R	0.001	0.014	-0.025	0.029	100	No
Volume of parsopercularis L	0.007	0.013	-0.019	0.032	100	No
Volume of parsopercularis R	-0.003	0.013	-0.026	0.022	100	No
Volume of parsorbitalis L	0.010	0.014	-0.015	0.038	100	No
Volume of parsorbitalis R	0.009	0.013	-0.018	0.034	100	No
Volume of parstriangularis L	0.005	0.013	-0.020	0.029	100	No
Volume of parstriangularis R	-0.001	0.013	-0.028	0.024	100	No
Volume of pericalcarine L	0.004	0.011	-0.018	0.027	100	No
Volume of pericalcarine R	0.002	0.012	-0.024	0.025	100	No
Volume of postcentral L	-0.019	0.013	-0.043	0.005	100	No
Volume of postcentral R	-0.005	0.012	-0.028	0.019	100	No
Volume of posteriorcingulate L	-0.023	0.012	-0.046	0.002	100	No
Volume of posteriorcingulate R	-0.021	0.012	-0.047	0.001	100	No
Volume of precentral L	-0.011	0.012	-0.035	0.013	100	No
Volume of precentral R	-0.007	0.011	-0.029	0.015	100	No
Volume of precuneus L	-0.007	0.012	-0.030	0.017	100	No
Volume of precuneus R	-0.003	0.011	-0.024	0.019	100	No
Volume of rostralanteriorcingulate L	-0.009	0.013	-0.035	0.015	100	No

Volume of rostralanteriorcingulate R	-0.005	0.013	-0.029	0.019	100	No
Volume of rostralmiddlefrontal L	-0.014	0.013	-0.039	0.010	100	No
Volume of rostralmiddlefrontal R	-0.003	0.012	-0.027	0.018	100	No
Volume of superiorfrontal L	-0.001	0.012	-0.026	0.022	100	No
Volume of superiorfrontal R	-0.007	0.013	-0.031	0.019	100	No
Volume of superiorparietal L	0.002	0.012	-0.022	0.027	100	No
Volume of superiorparietal R	-0.001	0.013	-0.027	0.025	100	No
Volume of superiortemporal L	0.004	0.013	-0.021	0.029	100	No
Volume of superiortemporal R	0.006	0.013	-0.019	0.031	100	No
Volume of supramarginal L	-0.002	0.013	-0.027	0.023	100	No
Volume of supramarginal R	-0.003	0.012	-0.025	0.019	100	No
Volume of transversetemporal L	-0.012	0.013	-0.037	0.012	100	No
Volume of transversetemporal R	-0.001	0.013	-0.027	0.022	100	No
Volume of accumbens L	-0.017	0.013	-0.043	0.010	100	No
Volume of accumbens R	-0.017	0.014	-0.044	0.011	100	No
Volume of amygdala L	-0.018	0.015	-0.046	0.011	100	No
Volume of amygdala R	-0.009	0.013	-0.036	0.016	100	No
Volume of caudate L	-0.016	0.013	-0.041	0.010	100	No
Volume of caudate R	-0.027	0.013	-0.053	0.000	100	No
Volume of hippocampus L	-0.008	0.012	-0.033	0.015	100	No
Volume of hippocampus R	-0.014	0.014	-0.041	0.013	100	No
Volume of pallidum L	-0.013	0.012	-0.036	0.011	100	No
Volume of pallidum R	-0.021	0.012	-0.045	0.004	100	No
Volume of putamen L	-0.015	0.013	-0.039	0.010	100	No
Volume of putamen R	-0.018	0.013	-0.044	0.009	100	No
Volume of thalamus L	-0.020	0.012	-0.044	0.005	100	No
Volume of thalamus R	-0.017	0.013	-0.042	0.009	100	No
Mean FA in anterior corona radiata L	-0.009	0.012	-0.034	0.014	100	No
Mean FA in anterior corona radiata R	-0.014	0.011	-0.036	0.008	100	No
Mean FA in anterior limb of internal capsule L	-0.017	0.011	-0.039	0.004	100	No
Mean FA in anterior limb of internal capsule R	-0.012	0.012	-0.036	0.011	100	No
Mean FA in body of corpus callosum	-0.034	0.012	-0.058	-0.011	100	Yes*
Mean FA in cerebral peduncle L	-0.014	0.012	-0.036	0.008	100	No
Mean FA in cerebral peduncle R	-0.018	0.012	-0.042	0.005	100	No
Mean FA in cingulum cingulate gyrus L	-0.002	0.011	-0.024	0.019	100	No
Mean FA in cingulum cingulate gyrus R	-0.007	0.011	-0.030	0.016	100	No
Mean FA in cingulum hippocampus L	0.004	0.012	-0.021	0.030	100	No
Mean FA in cingulum hippocampus R	0.009	0.012	-0.015	0.032	100	No
Mean FA in corticospinal tract L	0.014	0.014	-0.013	0.041	100	No
Mean FA in corticospinal tract R	0.010	0.013	-0.014	0.036	100	No
Mean FA in external capsule L	-0.004	0.011	-0.026	0.018	100	No
Mean FA in external capsule R	-0.002	0.012	-0.024	0.021	100	No
Mean FA in fornix cres+stria terminalis L	-0.007	0.012	-0.029	0.016	100	No
Mean FA in fornix cres+stria terminalis R	-0.010	0.013	-0.036	0.015	100	No

Mean FA in fornix	-0.028	0.012	-0.052	-0.006	100	Yes*
Mean FA in genu of corpus callosum	-0.022	0.012	-0.045	0.002	100	No
Mean FA in inferior cerebellar peduncle L	-0.017	0.012	-0.042	0.007	100	No
Mean FA in inferior cerebellar peduncle R	-0.017	0.012	-0.039	0.006	100	No
Mean FA in medial lemniscus L	-0.003	0.011	-0.025	0.019	100	No
Mean FA in medial lemniscus R	-0.004	0.011	-0.026	0.018	100	No
Mean FA in middle cerebellar peduncle	0.000	0.012	-0.022	0.024	100	No
Mean FA in pontine crossing tract	0.018	0.013	-0.009	0.044	100	No
Mean FA in posterior corona radiata L	0.001	0.012	-0.023	0.021	100	No
Mean FA in posterior corona radiata R	0.016	0.012	-0.007	0.041	100	No
Mean FA in posterior limb of internal capsule L	0.004	0.011	-0.020	0.026	100	No
Mean FA in posterior limb of internal capsule R	0.003	0.012	-0.022	0.025	100	No
Mean FA in posterior thalamic radiation L	-0.018	0.012	-0.040	0.006	100	No
Mean FA in posterior thalamic radiation R	-0.023	0.011	-0.045	-0.001	100	Yes*
Mean FA in retrolenticular part of internal capsule L	-0.009	0.013	-0.035	0.017	100	No
Mean FA in retrolenticular part of internal capsule R	0.004	0.012	-0.021	0.027	100	No
Mean FA in sagittal stratum L	-0.005	0.013	-0.030	0.019	100	No
Mean FA in sagittal stratum R	-0.011	0.011	-0.033	0.012	100	No
Mean FA in splenium of corpus callosum	0.001	0.012	-0.023	0.024	100	No
Mean FA in superior cerebellar peduncle L	-0.026	0.013	-0.052	-0.001	100	Yes*
Mean FA in superior cerebellar peduncle R	-0.017	0.014	-0.045	0.011	100	No
Mean FA in superior corona radiata L	0.002	0.011	-0.021	0.025	100	No
Mean FA in superior corona radiata R	0.010	0.013	-0.016	0.036	100	No
Mean FA in superior fronto-occipital fasciculus L	-0.024	0.012	-0.048	0.000	100	No
Mean FA in superior fronto-occipital fasciculus R	-0.012	0.012	-0.037	0.012	100	No
Mean FA in superior longitudinal fasciculus L	0.011	0.011	-0.009	0.033	100	No
Mean FA in superior longitudinal fasciculus R	0.026	0.012	0.003	0.049	100	Yes*
Mean FA in tapetum L	-0.005	0.013	-0.031	0.020	100	No
Mean FA in tapetum R	0.004	0.013	-0.023	0.030	100	No
Mean FA in uncinate fasciculus L	-0.004	0.011	-0.026	0.017	100	No
Mean FA in uncinate fasciculus R	0.001	0.012	-0.024	0.025	100	No
Mean L1 in anterior corona radiata L	-0.012	0.013	-0.037	0.013	100	No
Mean L1 in anterior corona radiata R	-0.011	0.012	-0.034	0.013	100	No
Mean L1 in anterior limb of internal capsule L	0.000	0.012	-0.025	0.022	100	No
Mean L1 in anterior limb of internal capsule R	0.014	0.012	-0.010	0.038	100	No
Mean L1 in body of corpus callosum	-0.033	0.013	-0.058	-0.007	100	Yes*
Mean L1 in cerebral peduncle L	-0.005	0.015	-0.035	0.022	100	No
Mean L1 in cerebral peduncle R	-0.018	0.016	-0.049	0.014	100	No
Mean L1 in cingulum cingulate gyrus L	-0.010	0.012	-0.034	0.013	100	No
Mean L1 in cingulum cingulate gyrus R	-0.004	0.012	-0.029	0.020	100	No
Mean L1 in cingulum hippocampus L	0.000	0.012	-0.021	0.024	100	No
Mean L1 in cingulum hippocampus R	-0.004	0.014	-0.029	0.024	100	No
Mean L1 in corticospinal tract L	0.006	0.013	-0.019	0.029	100	No
Mean L1 in corticospinal tract R	-0.005	0.013	-0.030	0.020	100	No

Mean L1 in external capsule L	0.003	0.012	-0.019	0.027	100	No
Mean L1 in external capsule R	0.002	0.012	-0.022	0.024	100	No
Mean L1 in fornix cres+stria terminalis L	0.005	0.012	-0.018	0.027	100	No
Mean L1 in fornix cres+stria terminalis R	-0.004	0.013	-0.028	0.022	100	No
Mean L1 in fornix	0.023	0.012	-0.001	0.047	100	No
Mean L1 in genu of corpus callosum	-0.034	0.014	-0.062	-0.008	100	Yes*
Mean L1 in inferior cerebellar peduncle L	-0.005	0.012	-0.030	0.019	100	No
Mean L1 in inferior cerebellar peduncle R	-0.009	0.013	-0.034	0.018	100	No
Mean L1 in medial lemniscus L	-0.003	0.012	-0.027	0.019	100	No
Mean L1 in medial lemniscus R	-0.008	0.012	-0.029	0.015	100	No
Mean L1 in middle cerebellar peduncle	-0.003	0.012	-0.026	0.021	100	No
Mean L1 in pontine crossing tract	-0.004	0.012	-0.027	0.018	100	No
Mean L1 in posterior corona radiata L	-0.003	0.011	-0.026	0.016	100	No
Mean L1 in posterior corona radiata R	0.006	0.011	-0.014	0.027	100	No
Mean L1 in posterior limb of internal capsule L	0.013	0.013	-0.011	0.037	100	No
Mean L1 in posterior limb of internal capsule R	0.013	0.013	-0.012	0.038	100	No
Mean L1 in posterior thalamic radiation L	-0.015	0.012	-0.038	0.010	100	No
Mean L1 in posterior thalamic radiation R	-0.031	0.012	-0.055	-0.009	100	Yes*
Mean L1 in retrolenticular part of internal capsule L	-0.005	0.013	-0.032	0.018	100	No
Mean L1 in retrolenticular part of internal capsule R	-0.009	0.013	-0.033	0.018	100	No
Mean L1 in sagittal stratum L	-0.013	0.011	-0.037	0.009	100	No
Mean L1 in sagittal stratum R	-0.017	0.012	-0.039	0.006	100	No
Mean L1 in splenium of corpus callosum	-0.005	0.013	-0.031	0.022	100	No
Mean L1 in superior cerebellar peduncle L	-0.014	0.012	-0.038	0.009	100	No
Mean L1 in superior cerebellar peduncle R	-0.012	0.013	-0.037	0.011	100	No
Mean L1 in superior corona radiata L	0.010	0.012	-0.013	0.034	100	No
Mean L1 in superior corona radiata R	0.009	0.012	-0.013	0.033	100	No
Mean L1 in superior fronto-occipital fasciculus L	-0.007	0.012	-0.033	0.018	100	No
Mean L1 in superior fronto-occipital fasciculus R	0.002	0.013	-0.024	0.026	100	No
Mean L1 in superior longitudinal fasciculus L	0.004	0.011	-0.017	0.026	100	No
Mean L1 in superior longitudinal fasciculus R	0.011	0.011	-0.010	0.034	100	No
Mean L1 in tapetum L	-0.004	0.014	-0.030	0.024	100	No
Mean L1 in tapetum R	-0.008	0.014	-0.032	0.020	100	No
Mean L1 in uncinate fasciculus L	0.005	0.013	-0.020	0.032	100	No
Mean L1 in uncinate fasciculus R	-0.007	0.012	-0.028	0.016	100	No
Mean RD in anterior corona radiata L	-0.001	0.010	-0.021	0.017	100	No
Mean RD in anterior corona radiata R	0.006	0.010	-0.013	0.025	100	No
Mean RD in anterior limb of internal capsule L	0.014	0.011	-0.010	0.036	100	No
Mean RD in anterior limb of internal capsule R	0.017	0.013	-0.007	0.042	100	No
Mean RD in body of corpus callosum	0.019	0.012	-0.005	0.044	100	No
Mean RD in cerebral peduncle L	0.014	0.012	-0.010	0.038	100	No
Mean RD in cerebral peduncle R	0.006	0.014	-0.019	0.034	100	No
Mean RD in cingulum cingulate gyrus L	-0.004	0.011	-0.026	0.017	100	No
Mean RD in cingulum cingulate gyrus R	0.005	0.011	-0.016	0.026	100	No

Mean RD in cingulum hippocampus L	-0.004	0.013	-0.028	0.020	100	No
Mean RD in cingulum hippocampus R	-0.009	0.012	-0.033	0.013	100	No
Mean RD in corticospinal tract L	-0.010	0.013	-0.034	0.015	100	No
Mean RD in corticospinal tract R	-0.010	0.012	-0.035	0.014	100	No
Mean RD in external capsule L	0.005	0.011	-0.018	0.027	100	No
Mean RD in external capsule R	0.003	0.011	-0.021	0.024	100	No
Mean RD in fornix cres+stria terminalis L	0.010	0.012	-0.016	0.032	100	No
Mean RD in fornix cres+stria terminalis R	0.010	0.013	-0.017	0.036	100	No
Mean RD in fornix	0.028	0.013	0.004	0.053	100	Yes*
Mean RD in genu of corpus callosum	0.010	0.012	-0.014	0.033	100	No
Mean RD in inferior cerebellar peduncle L	0.019	0.013	-0.007	0.044	100	No
Mean RD in inferior cerebellar peduncle R	0.019	0.012	-0.005	0.045	100	No
Mean RD in medial lemniscus L	-0.001	0.011	-0.023	0.020	100	No
Mean RD in medial lemniscus R	-0.002	0.011	-0.024	0.019	100	No
Mean RD in middle cerebellar peduncle	0.000	0.012	-0.023	0.023	100	No
Mean RD in pontine crossing tract	-0.017	0.012	-0.041	0.004	100	No
Mean RD in posterior corona radiata L	-0.003	0.010	-0.022	0.018	100	No
Mean RD in posterior corona radiata R	-0.015	0.010	-0.036	0.005	100	No
Mean RD in posterior limb of internal capsule L	0.001	0.012	-0.021	0.024	100	No
Mean RD in posterior limb of internal capsule R	0.002	0.012	-0.022	0.027	100	No
Mean RD in posterior thalamic radiation L	0.012	0.011	-0.011	0.033	100	No
Mean RD in posterior thalamic radiation R	0.009	0.010	-0.011	0.029	100	No
Mean RD in retrolenticular part of internal capsule L	0.006	0.012	-0.018	0.030	100	No
Mean RD in retrolenticular part of internal capsule R	-0.008	0.012	-0.031	0.016	100	No
Mean RD in sagittal stratum L	-0.003	0.012	-0.026	0.020	100	No
Mean RD in sagittal stratum R	0.003	0.011	-0.018	0.024	100	No
Mean RD in splenium of corpus callosum	-0.003	0.011	-0.024	0.021	100	No
Mean RD in superior cerebellar peduncle L	0.020	0.014	-0.008	0.048	100	No
Mean RD in superior cerebellar peduncle R	0.013	0.015	-0.014	0.042	100	No
Mean RD in superior corona radiata L	0.004	0.010	-0.017	0.024	100	No
Mean RD in superior corona radiata R	-0.005	0.011	-0.027	0.017	100	No
Mean RD in superior fronto-occipital fasciculus L	0.021	0.013	-0.005	0.045	100	No
Mean RD in superior fronto-occipital fasciculus R	0.014	0.012	-0.011	0.038	100	No
Mean RD in superior longitudinal fasciculus L	-0.016	0.010	-0.036	0.003	100	No
Mean RD in superior longitudinal fasciculus R	-0.025	0.011	-0.046	-0.004	100	Yes*
Mean RD in tapetum L	0.002	0.012	-0.022	0.026	100	No
Mean RD in tapetum R	-0.006	0.012	-0.029	0.017	100	No
Mean RD in uncinate fasciculus L	0.007	0.012	-0.017	0.030	100	No
Mean RD in uncinate fasciculus R	-0.005	0.012	-0.028	0.020	100	No
Spos_1	0.010	0.013	-0.016	0.034	100	No
Spos_2	-0.010	0.013	-0.037	0.014	100	No
Spos_3	-0.007	0.012	-0.030	0.017	100	No
Spos_4	0.008	0.014	-0.020	0.036	100	No
Spos_5	0.005	0.013	-0.022	0.031	100	No

Spos_6	-0.026	0.013	-0.052	0.001	100	No
Spos_7	-0.001	0.012	-0.025	0.022	100	No
Spos_8	-0.016	0.012	-0.041	0.006	100	No
Spos_9	-0.009	0.013	-0.036	0.016	100	No
Spos_10	-0.009	0.014	-0.037	0.020	100	No
Spos_11	-0.010	0.014	-0.038	0.017	100	No
Spos_12	-0.020	0.014	-0.048	0.007	100	No
Spos_13	-0.012	0.013	-0.038	0.011	100	No
Spos_14	-0.008	0.014	-0.034	0.018	100	No
Spos_15	-0.002	0.013	-0.027	0.024	100	No
Spos_16	-0.016	0.013	-0.041	0.008	100	No
Spos_17	-0.016	0.014	-0.042	0.011	100	No
Spos_18	0.010	0.014	-0.018	0.037	100	No
Spos_19	0.011	0.014	-0.016	0.036	100	No
Spos_20	-0.004	0.013	-0.031	0.021	100	No
Spos_21	0.002	0.014	-0.024	0.030	100	No
Spos_22	-0.006	0.014	-0.032	0.021	100	No
Spos_23	-0.020	0.013	-0.045	0.004	100	No
Spos_24	-0.009	0.014	-0.037	0.018	100	No
Spos_25	-0.006	0.014	-0.032	0.020	100	No
Spos_26	-0.007	0.014	-0.034	0.019	100	No
Spos_27	-0.009	0.012	-0.034	0.015	100	No
Spos_28	-0.009	0.013	-0.035	0.017	100	No
Spos_29	-0.006	0.014	-0.034	0.022	100	No
Spos_30	-0.007	0.012	-0.031	0.017	100	No
Spos_31	-0.013	0.014	-0.039	0.013	100	No
Spos_32	-0.010	0.013	-0.034	0.015	100	No
Spos_33	0.015	0.014	-0.013	0.043	100	No
Spos_34	0.011	0.014	-0.017	0.038	100	No
Spos_35	-0.012	0.014	-0.038	0.015	100	No
Spos_36	0.003	0.015	-0.026	0.032	100	No
Spos_37	-0.024	0.014	-0.051	0.002	100	No
Spos_38	0.002	0.014	-0.024	0.029	100	No
Spos_39	-0.007	0.013	-0.034	0.018	100	No
Spos_40	-0.002	0.014	-0.030	0.025	100	No
Spos_41	-0.020	0.012	-0.044	0.003	100	No
Spos_42	0.001	0.014	-0.026	0.028	100	No
Spos_43	-0.003	0.013	-0.028	0.022	100	No
Spos_44	-0.012	0.012	-0.038	0.011	100	No
Spos_45	0.009	0.015	-0.021	0.036	100	No
Spos_46	0.012	0.013	-0.013	0.038	100	No
Spos_47	-0.018	0.013	-0.045	0.006	100	No
Spos_48	-0.019	0.014	-0.045	0.007	100	No
Spos_49	-0.003	0.013	-0.029	0.022	100	No

Spos_50	-0.013	0.013	-0.038	0.012	100	No
Spos_51	0.011	0.014	-0.016	0.038	100	No
Spos_52	-0.016	0.014	-0.042	0.010	100	No
Spos_53	-0.013	0.012	-0.038	0.011	100	No
Spos_54	0.001	0.014	-0.026	0.028	100	No
Spos_55	0.010	0.014	-0.018	0.036	100	No
Sneg_1	0.007	0.012	-0.016	0.032	100	No
Sneg_2	-0.019	0.014	-0.046	0.008	100	No
Sneg_3	-0.008	0.012	-0.033	0.015	100	No
Sneg_4	-0.004	0.013	-0.030	0.022	100	No
Sneg_5	-0.006	0.014	-0.034	0.019	100	No
Sneg_6	-0.032	0.014	-0.059	-0.006	100	Yes*
Sneg_7	0.009	0.013	-0.017	0.035	100	No
Sneg_8	-0.006	0.013	-0.029	0.019	100	No
Sneg_9	-0.019	0.014	-0.045	0.008	100	No
Sneg_10	0.012	0.014	-0.014	0.039	100	No
Sneg_11	-0.022	0.014	-0.051	0.004	100	No
Sneg_12	0.001	0.015	-0.028	0.030	100	No
Sneg_13	-0.010	0.013	-0.036	0.015	100	No
Sneg_14	0.000	0.013	-0.026	0.025	100	No
Sneg_15	-0.014	0.013	-0.039	0.012	100	No
Sneg_16	-0.007	0.012	-0.030	0.018	100	No
Sneg_17	-0.016	0.014	-0.044	0.011	100	No
Sneg_18	-0.014	0.014	-0.042	0.014	100	No
Sneg_19	0.015	0.014	-0.012	0.042	100	No
Sneg_20	0.003	0.015	-0.027	0.032	100	No
Sneg_21	-0.015	0.013	-0.041	0.010	100	No
Sneg_22	-0.007	0.015	-0.037	0.022	100	No
Sneg_23	-0.010	0.014	-0.039	0.017	100	No
Sneg_24	-0.001	0.014	-0.028	0.026	100	No
Sneg_25	-0.007	0.014	-0.034	0.020	100	No
Sneg_26	-0.004	0.013	-0.031	0.022	100	No
Sneg_27	0.005	0.016	-0.025	0.036	100	No
Sneg_28	-0.006	0.013	-0.032	0.020	100	No
Sneg_29	-0.011	0.013	-0.037	0.013	100	No
Sneg_30	-0.007	0.013	-0.034	0.018	100	No
Sneg_31	-0.015	0.013	-0.040	0.010	100	No
Sneg_32	-0.008	0.013	-0.035	0.018	100	No
Sneg_33	0.001	0.014	-0.026	0.026	100	No
Sneg_34	-0.002	0.013	-0.027	0.024	100	No
Sneg_35	-0.016	0.013	-0.043	0.010	100	No
Sneg_36	0.016	0.013	-0.009	0.042	100	No
Sneg_37	0.001	0.014	-0.026	0.027	100	No
Sneg_38	-0.008	0.013	-0.033	0.017	100	No

Sneg_39	0.006	0.013	-0.018	0.032	100	No
Sneg_40	0.004	0.013	-0.023	0.030	100	No
Sneg_41	0.004	0.013	-0.022	0.028	100	No
Sneg_42	-0.023	0.015	-0.052	0.004	100	No
Sneg_43	-0.008	0.013	-0.033	0.018	100	No
Sneg_44	-0.021	0.013	-0.048	0.003	100	No
Sneg_45	0.005	0.014	-0.021	0.033	100	No
Sneg_46	0.007	0.013	-0.018	0.034	100	No
Sneg_47	0.003	0.014	-0.025	0.029	100	No
Sneg_48	-0.010	0.014	-0.036	0.016	100	No
Sneg_49	-0.011	0.014	-0.038	0.015	100	No
Sneg_50	-0.001	0.015	-0.031	0.029	100	No
Sneg_51	-0.014	0.013	-0.039	0.012	100	No
Sneg_52	-0.003	0.014	-0.029	0.023	100	No
Sneg_53	-0.002	0.013	-0.029	0.023	100	No
Sneg_54	-0.017	0.014	-0.045	0.009	100	No
Sneg_55	-0.010	0.015	-0.038	0.017	100	No
Median z-statistic (amygdala) for faces-shapes contrast	0.002	0.014	-0.027	0.027	100	No
Median z-statistic for faces activation	0.008	0.012	-0.013	0.032	100	No
Median z-statistic for shapes activation	0.000	0.012	-0.024	0.024	100	No
Median z-statistic for faces-shapes contrast	-0.001	0.013	-0.026	0.023	100	No
90th percentile of z-statistic (amygdala) for faces-shapes contrast	0.004	0.014	-0.024	0.030	100	No
90th percentile of z-statistic for faces activation	0.003	0.011	-0.019	0.025	100	No
90th percentile of z-statistic for shapes activation	0.000	0.012	-0.024	0.023	100	No
90th percentile of z-statistic for faces-shapes contrast	-0.004	0.012	-0.028	0.019	100	No
ALCDEP Walters2018	0.001	0.014	-0.027	0.028	100	No
AN Watson2019	0.006	0.015	-0.024	0.035	100	No
ASD Grove2019	0.010	0.013	-0.016	0.035	100	No
BD PGC4 2025	0.007	0.013	-0.019	0.034	100	No
BMI Locke2015	0.005	0.014	-0.022	0.032	100	No
Bngf Konieczny2025	-0.002	0.014	-0.030	0.025	100	No
CAD Nikpay2015	0.002	0.014	-0.026	0.030	100	No
CCL11 Konieczny2025	-0.026	0.014	-0.053	0.003	100	No
CCL2 Konieczny2025	0.002	0.014	-0.028	0.030	100	No
CCL3 Konieczny2025	-0.002	0.015	-0.029	0.027	100	No
CCL4 Konieczny2025	0.016	0.015	-0.012	0.046	100	No
CCL7 MCP3 Konieczny2025	-0.020	0.014	-0.047	0.006	100	No
CRP Said2022	0.004	0.012	-0.020	0.029	100	No
CSF1 Konieczny2025	-0.014	0.015	-0.044	0.013	100	No
CSF3 Konieczny2025	0.025	0.016	-0.006	0.058	100	No
CTACK Konieczny2025	0.009	0.012	-0.015	0.034	100	No
CUD Johnson2020	-0.015	0.015	-0.046	0.011	100	No
CXCL1 Konieczny2025	0.005	0.014	-0.024	0.032	100	No
CXCL10 Konieczny2025	0.002	0.014	-0.026	0.029	100	No

CXCL12 Konieczny2025	0.001	0.014	-0.027	0.028	100	No
CXCL9 Konieczny2025	0.000	0.013	-0.026	0.026	100	No
FGFb Konieczny2025	0.011	0.013	-0.017	0.037	100	No
GAD FinnGen2024	-0.017	0.014	-0.043	0.010	100	No
HbA1c Willems2023	0.018	0.014	-0.009	0.046	100	No
HDL Graham2021	-0.021	0.014	-0.048	0.005	100	No
HGF Konieczny2025	-0.019	0.013	-0.046	0.006	100	No
IFNg Konieczny2025	0.017	0.013	-0.010	0.043	100	No
IL10 Konieczny2025	0.020	0.013	-0.006	0.045	100	No
IL13 Konieczny2025	0.014	0.013	-0.010	0.040	100	No
IL16 Konieczny2025	0.000	0.013	-0.025	0.024	100	No
IL17 Konieczny2025	-0.001	0.012	-0.025	0.023	100	No
IL18 Konieczny2025	-0.008	0.015	-0.037	0.022	100	No
IL1b Konieczny2025	-0.011	0.015	-0.042	0.018	100	No
IL1RA Konieczny2025	-0.005	0.014	-0.034	0.020	100	No
IL2 Konieczny2025	0.007	0.015	-0.023	0.036	100	No
IL2RA Konieczny2025	0.020	0.014	-0.006	0.047	100	No
IL4 Konieczny2025	0.003	0.012	-0.021	0.024	100	No
IL5 Konieczny2025	0.011	0.012	-0.012	0.034	100	No
IL6 Konieczny2025	0.008	0.015	-0.021	0.036	100	No
IL7 Konieczny2025	-0.001	0.011	-0.024	0.022	100	No
IL8 Konieczny2025	0.016	0.015	-0.011	0.047	100	No
IL9 Konieczny2025	0.006	0.013	-0.018	0.031	100	No
LDL Graham2021	-0.010	0.014	-0.037	0.017	100	No
MDD PGC4_2025	0.002	0.014	-0.024	0.029	100	No
MIF Konieczny2025	0.026	0.014	0.000	0.057	100	Yes*
NEUROT DeMoor2015	0.014	0.014	-0.013	0.041	100	No
OCD PGC3 2018	-0.006	0.014	-0.034	0.022	100	No
PDGFb Konieczny2025	-0.010	0.016	-0.041	0.022	100	No
PTSD Nievergelt2024	0.007	0.014	-0.020	0.036	100	No
RANTES Konieczny2025	-0.011	0.014	-0.039	0.016	100	No
SCF Konieczny2025	-0.027	0.015	-0.059	0.003	100	No
SCGFb Konieczny2025	-0.001	0.014	-0.029	0.027	100	No
SCZ Trubetskoy2022	0.005	0.013	-0.019	0.030	100	No
T2D Verma2024	0.030	0.015	0.000	0.059	100	Yes*
TNFa Konieczny2025	0.010	0.012	-0.015	0.032	100	No
TNFb Konieczny2025	0.000	0.012	-0.023	0.026	100	No
TRAIL Konieczny2025	0.006	0.018	-0.029	0.042	100	No
TRIG Graham2021	0.018	0.014	-0.009	0.046	100	No
VEGF Konieczny2025	-0.001	0.013	-0.027	0.025	100	No

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CI, confidence interval; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte

growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; SD, standard deviation; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor; VIP, variable inclusion probability. *Statistical significance at 95%CI

Table A12. Bootstrap results of the elastic-net penalized regression model predicting diabetes within C11 of the multimodal stratification among the MDD sample of the UKB dataset.

Variable	Mean	SD	LowerCI	UpperCI	VIP	Significance
Area of caudalanteriorcingulate L	0.004	0.014	-0.028	0.029	100	No
Area of caudalanteriorcingulate R	0.001	0.018	-0.036	0.034	100	No
Area of caudalmiddlefrontal L	-0.011	0.016	-0.044	0.021	100	No
Area of caudalmiddlefrontal R	-0.010	0.016	-0.043	0.022	100	No
Area of cuneus L	-0.011	0.017	-0.046	0.021	100	No
Area of cuneus R	-0.008	0.015	-0.036	0.020	100	No
Area of entorhinal L	0.031	0.020	-0.007	0.072	100	No
Area of entorhinal R	0.003	0.017	-0.032	0.038	100	No
Area of fusiform L	0.021	0.015	-0.009	0.050	100	No
Area of fusiform R	0.015	0.016	-0.019	0.047	100	No
Area of inferiorparietal L	-0.005	0.015	-0.034	0.024	100	No
Area of inferiorparietal R	0.010	0.018	-0.024	0.044	100	No
Area of inferiortemporal L	-0.004	0.016	-0.037	0.027	100	No
Area of inferiortemporal R	-0.011	0.016	-0.042	0.021	100	No
Area of insula L	0.001	0.015	-0.028	0.032	100	No
Area of insula R	0.004	0.014	-0.023	0.032	100	No
Area of isthmuscingulate L	0.023	0.018	-0.011	0.060	100	No
Area of isthmuscingulate R	0.011	0.016	-0.020	0.042	100	No
Area of lateraloccipital L	0.012	0.015	-0.017	0.041	100	No
Area of lateraloccipital R	0.029	0.016	-0.001	0.063	100	No
Area of lateralorbitofrontal L	-0.040	0.016	-0.071	-0.010	100	Yes*
Area of lateralorbitofrontal R	-0.025	0.016	-0.057	0.007	100	No
Area of lingual L	0.003	0.015	-0.027	0.030	100	No
Area of lingual R	0.001	0.015	-0.028	0.030	100	No
Area of medialorbitofrontal L	-0.007	0.016	-0.036	0.023	100	No
Area of medialorbitofrontal R	-0.007	0.016	-0.039	0.026	100	No
Area of middletemporal L	-0.004	0.016	-0.033	0.027	100	No
Area of middletemporal R	-0.013	0.016	-0.042	0.018	100	No
Area of paracentral L	0.015	0.016	-0.017	0.046	100	No
Area of paracentral R	0.006	0.017	-0.028	0.038	100	No
Area of parahippocampal L	0.001	0.018	-0.035	0.035	100	No
Area of parahippocampal R	-0.013	0.017	-0.045	0.020	100	No
Area of parsopercularis L	-0.016	0.015	-0.047	0.013	100	No
Area of parsopercularis R	-0.007	0.016	-0.038	0.027	100	No
Area of parsorbitalis L	-0.003	0.016	-0.034	0.027	100	No
Area of parsorbitalis R	-0.001	0.018	-0.036	0.033	100	No
Area of parstriangularis L	-0.020	0.016	-0.055	0.011	100	No
Area of parstriangularis R	-0.013	0.016	-0.045	0.018	100	No
Area of pericalcarine L	-0.003	0.014	-0.032	0.025	100	No
Area of pericalcarine R	-0.010	0.015	-0.037	0.019	100	No
Area of postcentral L	0.015	0.015	-0.016	0.046	100	No

Area of postcentral R	0.003	0.017	-0.030	0.034	100	No
Area of posteriorcingulate L	0.001	0.015	-0.031	0.031	100	No
Area of posteriorcingulate R	0.018	0.016	-0.015	0.048	100	No
Area of precentral L	0.001	0.016	-0.032	0.033	100	No
Area of precentral R	0.005	0.015	-0.025	0.035	100	No
Area of precuneus L	0.004	0.015	-0.026	0.031	100	No
Area of precuneus R	0.004	0.015	-0.028	0.033	100	No
Area of rostralanteriorcingulate L	-0.005	0.016	-0.034	0.026	100	No
Area of rostralanteriorcingulate R	0.002	0.016	-0.030	0.034	100	No
Area of rostralmiddlefrontal L	-0.012	0.015	-0.040	0.016	100	No
Area of rostralmiddlefrontal R	-0.021	0.016	-0.050	0.012	100	No
Area of superiorfrontal L	0.009	0.015	-0.020	0.042	100	No
Area of superiorfrontal R	0.013	0.015	-0.017	0.046	100	No
Area of superiorparietal L	0.007	0.017	-0.025	0.042	100	No
Area of superiorparietal R	0.001	0.016	-0.032	0.031	100	No
Area of superiortemporal L	0.004	0.015	-0.024	0.034	100	No
Area of superiortemporal R	0.013	0.015	-0.017	0.042	100	No
Area of supramarginal L	-0.001	0.017	-0.034	0.033	100	No
Area of supramarginal R	-0.003	0.016	-0.036	0.029	100	No
Area of transversetemporal L	0.007	0.016	-0.023	0.039	100	No
Area of transversetemporal R	0.005	0.016	-0.029	0.036	100	No
Mean thickness of caudalanteriorcingulate L	0.003	0.016	-0.026	0.034	100	No
Mean thickness of caudalanteriorcingulate R	-0.029	0.017	-0.060	0.004	100	No
Mean thickness of caudalmiddlefrontal L	-0.027	0.014	-0.053	-0.001	100	Yes*
Mean thickness of caudalmiddlefrontal R	-0.021	0.015	-0.048	0.010	100	No
Mean thickness of cuneus L	-0.012	0.015	-0.042	0.017	100	No
Mean thickness of cuneus R	0.011	0.015	-0.017	0.042	100	No
Mean thickness of entorhinal L	0.009	0.019	-0.026	0.047	100	No
Mean thickness of entorhinal R	0.017	0.019	-0.022	0.057	100	No
Mean thickness of fusiform L	0.000	0.015	-0.028	0.028	100	No
Mean thickness of fusiform R	0.001	0.015	-0.028	0.029	100	No
Mean thickness of inferiorparietal L	-0.029	0.014	-0.056	0.001	100	No
Mean thickness of inferiorparietal R	-0.032	0.013	-0.058	-0.007	100	Yes*
Mean thickness of inferiortemporal L	-0.016	0.015	-0.045	0.012	100	No
Mean thickness of inferiortemporal R	-0.010	0.016	-0.043	0.020	100	No
Mean thickness of insula L	0.001	0.015	-0.026	0.031	100	No
Mean thickness of insula R	0.013	0.016	-0.018	0.045	100	No
Mean thickness of isthmuscingulate L	-0.004	0.017	-0.037	0.028	100	No
Mean thickness of isthmuscingulate R	-0.008	0.017	-0.041	0.025	100	No
Mean thickness of lateraloccipital L	-0.017	0.014	-0.043	0.009	100	No
Mean thickness of lateraloccipital R	-0.002	0.014	-0.030	0.026	100	No
Mean thickness of lateralorbitofrontal L	-0.008	0.016	-0.040	0.021	100	No
Mean thickness of lateralorbitofrontal R	0.000	0.015	-0.030	0.030	100	No
Mean thickness of lingual L	0.011	0.015	-0.018	0.042	100	No

Mean thickness of lingual R	0.008	0.015	-0.020	0.037	100	No
Mean thickness of medialorbitofrontal L	0.004	0.016	-0.027	0.036	100	No
Mean thickness of medialorbitofrontal R	0.005	0.017	-0.026	0.040	100	No
Mean thickness of middletemporal L	-0.018	0.015	-0.048	0.011	100	No
Mean thickness of middletemporal R	-0.002	0.014	-0.029	0.026	100	No
Mean thickness of paracentral L	-0.013	0.014	-0.039	0.015	100	No
Mean thickness of paracentral R	-0.019	0.015	-0.048	0.010	100	No
Mean thickness of parahippocampal L	0.009	0.016	-0.023	0.040	100	No
Mean thickness of parahippocampal R	-0.014	0.016	-0.047	0.017	100	No
Mean thickness of parsopercularis L	-0.006	0.015	-0.035	0.025	100	No
Mean thickness of parsopercularis R	-0.028	0.015	-0.058	-0.002	100	Yes*
Mean thickness of parsorbitalis L	-0.007	0.016	-0.038	0.024	100	No
Mean thickness of parsorbitalis R	-0.023	0.017	-0.056	0.010	100	No
Mean thickness of parstriangularis L	-0.008	0.016	-0.037	0.023	100	No
Mean thickness of parstriangularis R	-0.016	0.016	-0.046	0.016	100	No
Mean thickness of pericalcarine L	0.001	0.017	-0.033	0.032	100	No
Mean thickness of pericalcarine R	-0.007	0.016	-0.038	0.024	100	No
Mean thickness of postcentral L	-0.018	0.013	-0.044	0.007	100	No
Mean thickness of postcentral R	-0.018	0.015	-0.049	0.009	100	No
Mean thickness of posteriorcingulate L	0.001	0.016	-0.028	0.033	100	No
Mean thickness of posteriorcingulate R	-0.011	0.016	-0.042	0.019	100	No
Mean thickness of precentral L	-0.014	0.013	-0.038	0.014	100	No
Mean thickness of precentral R	-0.028	0.014	-0.053	0.001	100	No
Mean thickness of precuneus L	-0.028	0.014	-0.055	-0.001	100	Yes*
Mean thickness of precuneus R	-0.016	0.013	-0.041	0.008	100	No
Mean thickness of rostralanteriorcingulate L	-0.011	0.017	-0.045	0.021	100	No
Mean thickness of rostralanteriorcingulate R	-0.009	0.018	-0.044	0.027	100	No
Mean thickness of rostralmiddlefrontal L	-0.007	0.014	-0.035	0.019	100	No
Mean thickness of rostralmiddlefrontal R	-0.011	0.013	-0.038	0.017	100	No
Mean thickness of superiorfrontal L	-0.028	0.013	-0.053	-0.002	100	Yes*
Mean thickness of superiorfrontal R	-0.037	0.012	-0.060	-0.012	100	Yes*
Mean thickness of superiorparietal L	-0.023	0.014	-0.050	0.003	100	No
Mean thickness of superiorparietal R	-0.020	0.013	-0.048	0.004	100	No
Mean thickness of superiortemporal L	-0.009	0.013	-0.036	0.017	100	No
Mean thickness of superiortemporal R	-0.018	0.014	-0.045	0.012	100	No
Mean thickness of supramarginal L	-0.023	0.014	-0.049	0.003	100	No
Mean thickness of supramarginal R	-0.009	0.014	-0.037	0.018	100	No
Mean thickness of transversetemporal L	-0.008	0.017	-0.039	0.023	100	No
Mean thickness of transversetemporal R	-0.012	0.018	-0.049	0.023	100	No
Volume of caudalanteriorcingulate L	0.008	0.015	-0.021	0.038	100	No
Volume of caudalanteriorcingulate R	-0.010	0.017	-0.046	0.022	100	No
Volume of caudalmiddlefrontal L	-0.022	0.016	-0.052	0.010	100	No
Volume of caudalmiddlefrontal R	-0.018	0.016	-0.048	0.012	100	No
Volume of cuneus L	-0.013	0.016	-0.043	0.017	100	No

Volume of cuneus R	-0.001	0.015	-0.030	0.029	100	No
Volume of entorhinal L	0.033	0.018	-0.002	0.067	100	No
Volume of entorhinal R	0.018	0.018	-0.017	0.052	100	No
Volume of fusiform L	0.017	0.016	-0.014	0.047	100	No
Volume of fusiform R	0.011	0.016	-0.021	0.044	100	No
Volume of inferiorparietal L	-0.017	0.015	-0.046	0.013	100	No
Volume of inferiorparietal R	-0.007	0.017	-0.040	0.027	100	No
Volume of inferior temporal L	-0.010	0.016	-0.042	0.021	100	No
Volume of inferior temporal R	-0.020	0.016	-0.050	0.012	100	No
Volume of insula L	-0.007	0.015	-0.034	0.022	100	No
Volume of insula R	0.005	0.014	-0.021	0.033	100	No
Volume of isthmuscingulate L	0.016	0.018	-0.019	0.051	100	No
Volume of isthmuscingulate R	-0.006	0.016	-0.038	0.024	100	No
Volume of lateraloccipital L	-0.001	0.014	-0.029	0.026	100	No
Volume of lateraloccipital R	0.024	0.016	-0.006	0.058	100	No
Volume of lateralorbitofrontal L	-0.043	0.015	-0.072	-0.015	100	Yes*
Volume of lateralorbitofrontal R	-0.025	0.015	-0.053	0.006	100	No
Volume of lingual L	0.006	0.015	-0.023	0.036	100	No
Volume of lingual R	0.004	0.015	-0.024	0.035	100	No
Volume of medialorbitofrontal L	0.000	0.016	-0.032	0.030	100	No
Volume of medialorbitofrontal R	-0.009	0.015	-0.039	0.022	100	No
Volume of middletemporal L	-0.019	0.016	-0.050	0.012	100	No
Volume of middletemporal R	-0.021	0.016	-0.053	0.008	100	No
Volume of paracentral L	-0.001	0.016	-0.033	0.030	100	No
Volume of paracentral R	-0.004	0.018	-0.039	0.032	100	No
Volume of parahippocampal L	0.010	0.017	-0.023	0.042	100	No
Volume of parahippocampal R	-0.022	0.017	-0.057	0.011	100	No
Volume of parsopercularis L	-0.018	0.015	-0.049	0.011	100	No
Volume of parsopercularis R	-0.014	0.016	-0.046	0.018	100	No
Volume of parsorbitalis L	-0.006	0.016	-0.039	0.025	100	No
Volume of parsorbitalis R	-0.015	0.016	-0.047	0.017	100	No
Volume of parstriangularis L	-0.020	0.016	-0.054	0.012	100	No
Volume of parstriangularis R	-0.017	0.016	-0.047	0.014	100	No
Volume of pericalcarine L	0.001	0.015	-0.030	0.029	100	No
Volume of pericalcarine R	-0.010	0.015	-0.039	0.019	100	No
Volume of postcentral L	0.000	0.015	-0.029	0.029	100	No
Volume of postcentral R	-0.012	0.016	-0.043	0.019	100	No
Volume of posteriorcingulate L	0.007	0.017	-0.027	0.039	100	No
Volume of posteriorcingulate R	0.012	0.016	-0.018	0.044	100	No
Volume of precentral L	-0.004	0.016	-0.035	0.027	100	No
Volume of precentral R	-0.014	0.015	-0.045	0.015	100	No
Volume of precuneus L	-0.013	0.015	-0.043	0.015	100	No
Volume of precuneus R	-0.005	0.016	-0.038	0.025	100	No
Volume of rostralanteriorcingulate L	-0.011	0.017	-0.043	0.023	100	No

Volume of rostralanteriorcingulate R	-0.011	0.016	-0.043	0.022	100	No
Volume of rostralmiddlefrontal L	-0.014	0.015	-0.042	0.015	100	No
Volume of rostralmiddlefrontal R	-0.020	0.016	-0.050	0.011	100	No
Volume of superiorfrontal L	-0.007	0.015	-0.036	0.023	100	No
Volume of superiorfrontal R	-0.002	0.015	-0.033	0.028	100	No
Volume of superiorparietal L	-0.007	0.016	-0.037	0.025	100	No
Volume of superiorparietal R	-0.011	0.016	-0.043	0.018	100	No
Volume of superiortemporal L	-0.004	0.015	-0.032	0.024	100	No
Volume of superiortemporal R	-0.001	0.015	-0.030	0.028	100	No
Volume of supramarginal L	-0.011	0.018	-0.046	0.023	100	No
Volume of supramarginal R	-0.008	0.016	-0.041	0.025	100	No
Volume of transversetemporal L	0.001	0.016	-0.030	0.034	100	No
Volume of transversetemporal R	0.006	0.017	-0.029	0.038	100	No
Volume of accumbens L	-0.009	0.017	-0.040	0.023	100	No
Volume of accumbens R	-0.012	0.016	-0.045	0.019	100	No
Volume of amygdala L	0.001	0.021	-0.040	0.042	100	No
Volume of amygdala R	-0.014	0.021	-0.059	0.026	100	No
Volume of caudate L	-0.033	0.018	-0.070	-0.001	100	Yes*
Volume of caudate R	-0.025	0.019	-0.062	0.011	100	No
Volume of hippocampus L	-0.019	0.018	-0.054	0.015	100	No
Volume of hippocampus R	-0.005	0.018	-0.042	0.029	100	No
Volume of pallidum L	-0.014	0.018	-0.049	0.021	100	No
Volume of pallidum R	-0.023	0.017	-0.057	0.010	100	No
Volume of putamen L	-0.019	0.018	-0.052	0.015	100	No
Volume of putamen R	-0.018	0.017	-0.052	0.013	100	No
Volume of thalamus L	-0.028	0.016	-0.058	0.004	100	No
Volume of thalamus R	-0.030	0.015	-0.058	0.000	100	Yes*
Mean FA in anterior corona radiata L	-0.011	0.014	-0.039	0.017	100	No
Mean FA in anterior corona radiata R	-0.005	0.014	-0.033	0.022	100	No
Mean FA in anterior limb of internal capsule L	0.005	0.016	-0.027	0.036	100	No
Mean FA in anterior limb of internal capsule R	0.019	0.016	-0.012	0.050	100	No
Mean FA in body of corpus callosum	-0.022	0.014	-0.049	0.006	100	No
Mean FA in cerebral peduncle L	0.001	0.015	-0.027	0.031	100	No
Mean FA in cerebral peduncle R	-0.007	0.016	-0.037	0.024	100	No
Mean FA in cingulum cingulate gyrus L	-0.002	0.014	-0.029	0.026	100	No
Mean FA in cingulum cingulate gyrus R	-0.003	0.014	-0.031	0.024	100	No
Mean FA in cingulum hippocampus L	0.025	0.015	-0.005	0.055	100	No
Mean FA in cingulum hippocampus R	0.023	0.015	-0.008	0.054	100	No
Mean FA in corticospinal tract L	0.009	0.019	-0.026	0.045	100	No
Mean FA in corticospinal tract R	0.008	0.017	-0.025	0.042	100	No
Mean FA in external capsule L	0.006	0.015	-0.025	0.037	100	No
Mean FA in external capsule R	-0.005	0.015	-0.034	0.024	100	No
Mean FA in fornix cres+stria terminalis L	-0.013	0.015	-0.044	0.014	100	No
Mean FA in fornix cres+stria terminalis R	-0.006	0.015	-0.034	0.024	100	No

Mean FA in fornix	-0.013	0.014	-0.041	0.015	100	No
Mean FA in genu of corpus callosum	-0.028	0.014	-0.055	0.000	100	No
Mean FA in inferior cerebellar peduncle L	-0.005	0.015	-0.034	0.022	100	No
Mean FA in inferior cerebellar peduncle R	-0.007	0.015	-0.038	0.023	100	No
Mean FA in medial lemniscus L	0.013	0.015	-0.018	0.043	100	No
Mean FA in medial lemniscus R	-0.002	0.017	-0.033	0.030	100	No
Mean FA in middle cerebellar peduncle	0.015	0.015	-0.013	0.045	100	No
Mean FA in pontine crossing tract	0.009	0.018	-0.027	0.043	100	No
Mean FA in posterior corona radiata L	0.000	0.014	-0.028	0.027	100	No
Mean FA in posterior corona radiata R	0.000	0.014	-0.028	0.028	100	No
Mean FA in posterior limb of internal capsule L	-0.015	0.015	-0.043	0.013	100	No
Mean FA in posterior limb of internal capsule R	0.006	0.014	-0.020	0.032	100	No
Mean FA in posterior thalamic radiation L	-0.001	0.014	-0.028	0.024	100	No
Mean FA in posterior thalamic radiation R	-0.010	0.015	-0.039	0.018	100	No
Mean FA in retrolenticular part of internal capsule L	-0.020	0.014	-0.047	0.009	100	No
Mean FA in retrolenticular part of internal capsule R	-0.003	0.015	-0.031	0.025	100	No
Mean FA in sagittal stratum L	-0.005	0.015	-0.034	0.024	100	No
Mean FA in sagittal stratum R	-0.001	0.016	-0.033	0.030	100	No
Mean FA in splenium of corpus callosum	0.000	0.015	-0.029	0.030	100	No
Mean FA in superior cerebellar peduncle L	-0.018	0.015	-0.047	0.011	100	No
Mean FA in superior cerebellar peduncle R	-0.015	0.015	-0.046	0.014	100	No
Mean FA in superior corona radiata L	0.003	0.015	-0.027	0.031	100	No
Mean FA in superior corona radiata R	0.008	0.015	-0.021	0.037	100	No
Mean FA in superior fronto-occipital fasciculus L	-0.019	0.015	-0.048	0.009	100	No
Mean FA in superior fronto-occipital fasciculus R	-0.022	0.016	-0.054	0.008	100	No
Mean FA in superior longitudinal fasciculus L	0.009	0.015	-0.022	0.037	100	No
Mean FA in superior longitudinal fasciculus R	0.006	0.014	-0.020	0.036	100	No
Mean FA in tapetum L	0.004	0.016	-0.027	0.034	100	No
Mean FA in tapetum R	-0.003	0.017	-0.035	0.027	100	No
Mean FA in uncinate fasciculus L	-0.001	0.016	-0.032	0.030	100	No
Mean FA in uncinate fasciculus R	0.000	0.017	-0.032	0.032	100	No
Mean L1 in anterior corona radiata L	-0.002	0.015	-0.031	0.026	100	No
Mean L1 in anterior corona radiata R	0.003	0.015	-0.024	0.032	100	No
Mean L1 in anterior limb of internal capsule L	0.001	0.015	-0.028	0.032	100	No
Mean L1 in anterior limb of internal capsule R	-0.001	0.017	-0.034	0.032	100	No
Mean L1 in body of corpus callosum	0.007	0.017	-0.025	0.041	100	No
Mean L1 in cerebral peduncle L	-0.003	0.017	-0.036	0.031	100	No
Mean L1 in cerebral peduncle R	0.009	0.017	-0.024	0.045	100	No
Mean L1 in cingulum cingulate gyrus L	0.001	0.016	-0.029	0.030	100	No
Mean L1 in cingulum cingulate gyrus R	-0.008	0.016	-0.041	0.023	100	No
Mean L1 in cingulum hippocampus L	0.014	0.016	-0.017	0.047	100	No
Mean L1 in cingulum hippocampus R	0.009	0.016	-0.022	0.041	100	No
Mean L1 in corticospinal tract L	-0.002	0.016	-0.033	0.030	100	No
Mean L1 in corticospinal tract R	0.000	0.016	-0.029	0.031	100	No

Mean L1 in external capsule L	0.013	0.016	-0.019	0.044	100	No
Mean L1 in external capsule R	0.013	0.015	-0.019	0.043	100	No
Mean L1 in fornix cres+stria terminalis L	0.009	0.017	-0.025	0.042	100	No
Mean L1 in fornix cres+stria terminalis R	0.010	0.017	-0.023	0.044	100	No
Mean L1 in fornix	0.001	0.014	-0.028	0.028	100	No
Mean L1 in genu of corpus callosum	-0.012	0.019	-0.046	0.024	100	No
Mean L1 in inferior cerebellar peduncle L	0.002	0.017	-0.030	0.035	100	No
Mean L1 in inferior cerebellar peduncle R	-0.003	0.017	-0.034	0.029	100	No
Mean L1 in medial lemniscus L	-0.003	0.014	-0.033	0.025	100	No
Mean L1 in medial lemniscus R	0.007	0.015	-0.025	0.038	100	No
Mean L1 in middle cerebellar peduncle	0.017	0.016	-0.012	0.049	100	No
Mean L1 in pontine crossing tract	-0.011	0.013	-0.037	0.017	100	No
Mean L1 in posterior corona radiata L	-0.003	0.013	-0.027	0.022	100	No
Mean L1 in posterior corona radiata R	0.000	0.013	-0.026	0.023	100	No
Mean L1 in posterior limb of internal capsule L	0.011	0.015	-0.019	0.040	100	No
Mean L1 in posterior limb of internal capsule R	0.012	0.015	-0.017	0.041	100	No
Mean L1 in posterior thalamic radiation L	-0.008	0.015	-0.038	0.021	100	No
Mean L1 in posterior thalamic radiation R	-0.026	0.016	-0.059	0.004	100	No
Mean L1 in retrolenticular part of internal capsule L	-0.001	0.015	-0.029	0.029	100	No
Mean L1 in retrolenticular part of internal capsule R	-0.005	0.015	-0.035	0.024	100	No
Mean L1 in sagittal stratum L	0.002	0.015	-0.027	0.031	100	No
Mean L1 in sagittal stratum R	-0.002	0.015	-0.030	0.028	100	No
Mean L1 in splenium of corpus callosum	-0.008	0.016	-0.039	0.023	100	No
Mean L1 in superior cerebellar peduncle L	0.019	0.016	-0.012	0.048	100	No
Mean L1 in superior cerebellar peduncle R	0.010	0.015	-0.020	0.040	100	No
Mean L1 in superior corona radiata L	0.006	0.014	-0.020	0.034	100	No
Mean L1 in superior corona radiata R	0.003	0.014	-0.025	0.032	100	No
Mean L1 in superior fronto-occipital fasciculus L	0.007	0.017	-0.026	0.039	100	No
Mean L1 in superior fronto-occipital fasciculus R	0.004	0.016	-0.026	0.035	100	No
Mean L1 in superior longitudinal fasciculus L	-0.007	0.013	-0.034	0.017	100	No
Mean L1 in superior longitudinal fasciculus R	-0.031	0.016	-0.062	0.000	100	No
Mean L1 in tapetum L	-0.009	0.018	-0.044	0.027	100	No
Mean L1 in tapetum R	-0.005	0.016	-0.039	0.026	100	No
Mean L1 in uncinate fasciculus L	0.013	0.016	-0.018	0.044	100	No
Mean L1 in uncinate fasciculus R	0.001	0.017	-0.032	0.033	100	No
Mean RD in anterior corona radiata L	0.007	0.012	-0.016	0.033	100	No
Mean RD in anterior corona radiata R	0.005	0.012	-0.020	0.030	100	No
Mean RD in anterior limb of internal capsule L	-0.005	0.015	-0.034	0.024	100	No
Mean RD in anterior limb of internal capsule R	-0.023	0.016	-0.055	0.008	100	No
Mean RD in body of corpus callosum	0.024	0.014	-0.005	0.052	100	No
Mean RD in cerebral peduncle L	0.000	0.016	-0.033	0.029	100	No
Mean RD in cerebral peduncle R	0.009	0.017	-0.026	0.042	100	No
Mean RD in cingulum cingulate gyrus L	0.006	0.014	-0.022	0.033	100	No
Mean RD in cingulum cingulate gyrus R	0.004	0.016	-0.026	0.034	100	No

Mean RD in cingulum hippocampus L	-0.019	0.015	-0.052	0.011	100	No
Mean RD in cingulum hippocampus R	-0.020	0.016	-0.052	0.011	100	No
Mean RD in corticospinal tract L	-0.016	0.015	-0.044	0.013	100	No
Mean RD in corticospinal tract R	-0.008	0.014	-0.036	0.019	100	No
Mean RD in external capsule L	0.004	0.016	-0.026	0.036	100	No
Mean RD in external capsule R	0.013	0.015	-0.016	0.041	100	No
Mean RD in fornix cres+stria terminalis L	0.017	0.014	-0.010	0.046	100	No
Mean RD in fornix cres+stria terminalis R	0.009	0.014	-0.019	0.036	100	No
Mean RD in fornix	0.003	0.014	-0.026	0.031	100	No
Mean RD in genu of corpus callosum	0.023	0.014	-0.005	0.050	100	No
Mean RD in inferior cerebellar peduncle L	0.006	0.016	-0.027	0.038	100	No
Mean RD in inferior cerebellar peduncle R	0.010	0.016	-0.021	0.043	100	No
Mean RD in medial lemniscus L	-0.010	0.013	-0.036	0.017	100	No
Mean RD in medial lemniscus R	0.006	0.015	-0.023	0.034	100	No
Mean RD in middle cerebellar peduncle	-0.002	0.014	-0.030	0.025	100	No
Mean RD in pontine crossing tract	-0.016	0.014	-0.045	0.013	100	No
Mean RD in posterior corona radiata L	-0.004	0.011	-0.027	0.017	100	No
Mean RD in posterior corona radiata R	-0.003	0.012	-0.027	0.021	100	No
Mean RD in posterior limb of internal capsule L	0.019	0.016	-0.011	0.050	100	No
Mean RD in posterior limb of internal capsule R	-0.002	0.015	-0.030	0.026	100	No
Mean RD in posterior thalamic radiation L	-0.002	0.011	-0.023	0.019	100	No
Mean RD in posterior thalamic radiation R	-0.002	0.013	-0.026	0.022	100	No
Mean RD in retrolenticular part of internal capsule L	0.020	0.014	-0.007	0.047	100	No
Mean RD in retrolenticular part of internal capsule R	0.002	0.014	-0.025	0.028	100	No
Mean RD in sagittal stratum L	0.005	0.014	-0.022	0.033	100	No
Mean RD in sagittal stratum R	0.002	0.014	-0.025	0.029	100	No
Mean RD in splenium of corpus callosum	-0.005	0.014	-0.035	0.022	100	No
Mean RD in superior cerebellar peduncle L	0.027	0.014	-0.001	0.056	100	No
Mean RD in superior cerebellar peduncle R	0.019	0.015	-0.009	0.050	100	No
Mean RD in superior corona radiata L	-0.004	0.012	-0.027	0.019	100	No
Mean RD in superior corona radiata R	-0.008	0.013	-0.035	0.017	100	No
Mean RD in superior fronto-occipital fasciculus L	0.017	0.016	-0.015	0.046	100	No
Mean RD in superior fronto-occipital fasciculus R	0.019	0.014	-0.009	0.046	100	No
Mean RD in superior longitudinal fasciculus L	-0.015	0.014	-0.041	0.012	100	No
Mean RD in superior longitudinal fasciculus R	-0.021	0.014	-0.048	0.005	100	No
Mean RD in tapetum L	-0.008	0.015	-0.040	0.022	100	No
Mean RD in tapetum R	-0.001	0.015	-0.031	0.029	100	No
Mean RD in uncinate fasciculus L	0.010	0.016	-0.021	0.040	100	No
Mean RD in uncinate fasciculus R	0.000	0.016	-0.030	0.031	100	No
Spos_1	-0.009	0.016	-0.042	0.022	100	No
Spos_2	0.015	0.018	-0.019	0.053	100	No
Spos_3	-0.001	0.016	-0.033	0.032	100	No
Spos_4	0.043	0.018	0.008	0.079	100	Yes*
Spos_5	-0.025	0.020	-0.064	0.014	100	No

Spos_6	0.017	0.017	-0.017	0.051	100	No
Spos_7	-0.016	0.018	-0.050	0.018	100	No
Spos_8	-0.013	0.016	-0.046	0.019	100	No
Spos_9	0.006	0.018	-0.027	0.039	100	No
Spos_10	-0.004	0.020	-0.041	0.036	100	No
Spos_11	0.003	0.018	-0.033	0.037	100	No
Spos_12	0.020	0.019	-0.017	0.059	100	No
Spos_13	-0.012	0.018	-0.047	0.023	100	No
Spos_14	0.005	0.018	-0.030	0.038	100	No
Spos_15	0.002	0.018	-0.032	0.038	100	No
Spos_16	-0.029	0.017	-0.062	0.004	100	No
Spos_17	0.000	0.019	-0.038	0.040	100	No
Spos_18	0.004	0.019	-0.035	0.042	100	No
Spos_19	0.000	0.019	-0.037	0.038	100	No
Spos_20	0.008	0.018	-0.026	0.043	100	No
Spos_21	0.014	0.018	-0.019	0.048	100	No
Spos_22	0.006	0.018	-0.027	0.042	100	No
Spos_23	-0.006	0.019	-0.045	0.031	100	No
Spos_24	0.017	0.018	-0.017	0.053	100	No
Spos_25	0.032	0.018	-0.005	0.069	100	No
Spos_26	0.017	0.019	-0.021	0.053	100	No
Spos_27	0.019	0.018	-0.014	0.054	100	No
Spos_28	0.014	0.019	-0.022	0.048	100	No
Spos_29	-0.013	0.021	-0.053	0.028	100	No
Spos_30	0.003	0.018	-0.035	0.036	100	No
Spos_31	-0.006	0.019	-0.046	0.029	100	No
Spos_32	-0.001	0.017	-0.037	0.031	100	No
Spos_33	-0.010	0.018	-0.046	0.026	100	No
Spos_34	0.005	0.019	-0.032	0.041	100	No
Spos_35	0.005	0.017	-0.028	0.039	100	No
Spos_36	-0.017	0.019	-0.054	0.017	100	No
Spos_37	-0.012	0.017	-0.044	0.021	100	No
Spos_38	0.007	0.019	-0.028	0.046	100	No
Spos_39	0.018	0.022	-0.022	0.061	100	No
Spos_40	0.012	0.018	-0.024	0.050	100	No
Spos_41	0.009	0.018	-0.025	0.046	100	No
Spos_42	-0.006	0.019	-0.042	0.033	100	No
Spos_43	-0.022	0.019	-0.059	0.013	100	No
Spos_44	0.010	0.017	-0.023	0.045	100	No
Spos_45	-0.013	0.017	-0.048	0.018	100	No
Spos_46	0.000	0.019	-0.035	0.038	100	No
Spos_47	0.000	0.018	-0.035	0.036	100	No
Spos_48	-0.012	0.020	-0.052	0.025	100	No
Spos_49	-0.013	0.018	-0.049	0.022	100	No

Spos_50	0.010	0.020	-0.028	0.050	100	No
Spos_51	-0.020	0.018	-0.056	0.013	100	No
Spos_52	0.002	0.018	-0.037	0.037	100	No
Spos_53	-0.009	0.018	-0.042	0.026	100	No
Spos_54	-0.019	0.019	-0.058	0.018	100	No
Spos_55	0.005	0.020	-0.035	0.045	100	No
Sneg_1	-0.017	0.017	-0.051	0.016	100	No
Sneg_2	-0.002	0.019	-0.043	0.036	100	No
Sneg_3	0.004	0.018	-0.030	0.041	100	No
Sneg_4	-0.021	0.017	-0.055	0.012	100	No
Sneg_5	0.008	0.019	-0.028	0.044	100	No
Sneg_6	-0.006	0.018	-0.043	0.029	100	No
Sneg_7	-0.031	0.018	-0.065	0.003	100	No
Sneg_8	0.004	0.017	-0.030	0.038	100	No
Sneg_9	0.024	0.021	-0.017	0.066	100	No
Sneg_10	-0.010	0.019	-0.044	0.026	100	No
Sneg_11	-0.021	0.018	-0.056	0.015	100	No
Sneg_12	-0.034	0.019	-0.073	0.003	100	No
Sneg_13	-0.010	0.018	-0.047	0.026	100	No
Sneg_14	-0.017	0.016	-0.050	0.014	100	No
Sneg_15	-0.019	0.017	-0.050	0.014	100	No
Sneg_16	-0.012	0.017	-0.045	0.023	100	No
Sneg_17	0.001	0.019	-0.036	0.039	100	No
Sneg_18	-0.019	0.018	-0.053	0.016	100	No
Sneg_19	-0.005	0.020	-0.046	0.034	100	No
Sneg_20	-0.009	0.017	-0.044	0.025	100	No
Sneg_21	-0.015	0.018	-0.049	0.021	100	No
Sneg_22	0.004	0.020	-0.037	0.041	100	No
Sneg_23	-0.003	0.019	-0.040	0.031	100	No
Sneg_24	-0.004	0.019	-0.041	0.033	100	No
Sneg_25	0.008	0.018	-0.027	0.045	100	No
Sneg_26	-0.022	0.019	-0.060	0.014	100	No
Sneg_27	-0.002	0.018	-0.035	0.037	100	No
Sneg_28	-0.008	0.018	-0.044	0.030	100	No
Sneg_29	-0.002	0.019	-0.039	0.036	100	No
Sneg_30	-0.017	0.018	-0.056	0.016	100	No
Sneg_31	-0.027	0.019	-0.063	0.009	100	No
Sneg_32	-0.016	0.017	-0.049	0.017	100	No
Sneg_33	-0.022	0.018	-0.059	0.014	100	No
Sneg_34	0.014	0.020	-0.025	0.053	100	No
Sneg_35	-0.036	0.019	-0.075	-0.001	100	Yes*
Sneg_36	0.004	0.018	-0.030	0.039	100	No
Sneg_37	-0.022	0.019	-0.058	0.017	100	No
Sneg_38	-0.026	0.018	-0.063	0.009	100	No

Sneg_39	0.006	0.018	-0.031	0.039	100	No
Sneg_40	-0.008	0.021	-0.052	0.032	100	No
Sneg_41	0.004	0.018	-0.031	0.040	100	No
Sneg_42	-0.026	0.017	-0.059	0.007	100	No
Sneg_43	0.015	0.019	-0.023	0.050	100	No
Sneg_44	-0.020	0.018	-0.055	0.016	100	No
Sneg_45	-0.005	0.018	-0.040	0.031	100	No
Sneg_46	0.008	0.019	-0.030	0.045	100	No
Sneg_47	-0.002	0.020	-0.040	0.035	100	No
Sneg_48	0.005	0.019	-0.032	0.045	100	No
Sneg_49	-0.005	0.018	-0.041	0.028	100	No
Sneg_50	0.004	0.020	-0.036	0.043	100	No
Sneg_51	-0.016	0.018	-0.055	0.017	100	No
Sneg_52	-0.016	0.018	-0.052	0.021	100	No
Sneg_53	0.009	0.018	-0.026	0.044	100	No
Sneg_54	0.023	0.019	-0.016	0.060	100	No
Sneg_55	-0.004	0.020	-0.042	0.035	100	No
Median z-statistic (amygdala) for faces-shapes contrast	-0.012	0.017	-0.045	0.021	100	No
Median z-statistic for faces activation	0.003	0.016	-0.028	0.033	100	No
Median z-statistic for shapes activation	0.001	0.016	-0.031	0.030	100	No
Median z-statistic for faces-shapes contrast	0.003	0.016	-0.028	0.033	100	No
90th percentile of z-statistic (amygdala) for faces-shapes contrast	-0.017	0.017	-0.048	0.017	100	No
90th percentile of z-statistic for faces activation	0.000	0.015	-0.029	0.029	100	No
90th percentile of z-statistic for shapes activation	-0.001	0.016	-0.033	0.031	100	No
90th percentile of z-statistic for faces-shapes contrast	0.007	0.016	-0.025	0.038	100	No
ALCDEP Walters2018	-0.011	0.018	-0.048	0.024	100	No
AN Watson2019	-0.020	0.020	-0.058	0.018	100	No
ASD Grove2019	0.004	0.018	-0.034	0.039	100	No
BD PGC4 2025	-0.021	0.021	-0.061	0.018	100	No
BMI Locke2015	-0.002	0.020	-0.043	0.035	100	No
Bngf Konieczny2025	0.004	0.018	-0.030	0.038	100	No
CAD Nikpay2015	0.026	0.019	-0.014	0.063	100	No
CCL11 Konieczny2025	0.008	0.019	-0.031	0.046	100	No
CCL2 Konieczny2025	0.045	0.021	0.005	0.087	100	Yes*
CCL3 Konieczny2025	0.012	0.019	-0.027	0.048	100	No
CCL4 Konieczny2025	0.000	0.019	-0.035	0.039	100	No
CCL7 MCP3 Konieczny2025	-0.001	0.019	-0.036	0.038	100	No
CRP Said2022	0.013	0.019	-0.025	0.051	100	No
CSF1 Konieczny2025	0.013	0.019	-0.023	0.051	100	No
CSF3 Konieczny2025	0.019	0.019	-0.018	0.057	100	No
CTACK Konieczny2025	-0.003	0.017	-0.035	0.032	100	No
CUD Johnson2020	-0.016	0.020	-0.055	0.023	100	No
CXCL1 Konieczny2025	0.027	0.021	-0.011	0.070	100	No
CXCL10 Konieczny2025	0.015	0.019	-0.022	0.050	100	No

CXCL12 Konieczny2025	0.009	0.019	-0.028	0.044	100	No
CXCL9 Konieczny2025	0.004	0.018	-0.034	0.037	100	No
FGFb Konieczny2025	0.005	0.019	-0.033	0.042	100	No
GAD FinnGen2024	-0.001	0.018	-0.034	0.033	100	No
HbA1c Willems2023	0.024	0.020	-0.012	0.065	100	No
HDL Graham2021	-0.018	0.021	-0.063	0.022	100	No
HGF Konieczny2025	0.004	0.020	-0.035	0.044	100	No
IFNg Konieczny2025	0.011	0.016	-0.022	0.043	100	No
IL10 Konieczny2025	0.000	0.017	-0.035	0.033	100	No
IL13 Konieczny2025	0.001	0.015	-0.027	0.031	100	No
IL16 Konieczny2025	-0.005	0.021	-0.046	0.037	100	No
IL17 Konieczny2025	0.028	0.017	-0.005	0.061	100	No
IL18 Konieczny2025	-0.007	0.020	-0.044	0.035	100	No
IL1b Konieczny2025	-0.016	0.021	-0.058	0.024	100	No
IL1RA Konieczny2025	0.005	0.018	-0.032	0.039	100	No
IL2 Konieczny2025	0.012	0.019	-0.026	0.048	100	No
IL2RA Konieczny2025	-0.034	0.019	-0.070	0.004	100	No
IL4 Konieczny2025	0.020	0.017	-0.012	0.051	100	No
IL5 Konieczny2025	0.014	0.016	-0.020	0.043	100	No
IL6 Konieczny2025	0.014	0.018	-0.023	0.050	100	No
IL7 Konieczny2025	0.020	0.016	-0.011	0.052	100	No
IL8 Konieczny2025	0.019	0.017	-0.013	0.053	100	No
IL9 Konieczny2025	0.018	0.018	-0.016	0.053	100	No
LDL Graham2021	-0.007	0.021	-0.048	0.034	100	No
MDD PGC4_2025	0.006	0.020	-0.031	0.045	100	No
MIF Konieczny2025	-0.030	0.019	-0.068	0.008	100	No
NEUROT DeMoor2015	-0.010	0.020	-0.048	0.029	100	No
OCD PGC3 2018	0.014	0.019	-0.027	0.051	100	No
PDGFBB Konieczny2025	-0.001	0.019	-0.038	0.035	100	No
PTSD Nievergelt2024	0.017	0.019	-0.019	0.055	100	No
RANTES Konieczny2025	-0.009	0.020	-0.046	0.030	100	No
SCF Konieczny2025	-0.005	0.020	-0.045	0.032	100	No
SCGFb Konieczny2025	-0.001	0.019	-0.036	0.034	100	No
SCZ Trubetskoy2022	-0.028	0.020	-0.065	0.010	100	No
T2D Verma2024	0.053	0.020	0.014	0.095	100	Yes*
TNFa Konieczny2025	0.017	0.016	-0.015	0.049	100	No
TNFb Konieczny2025	0.011	0.014	-0.017	0.037	100	No
TRAIL Konieczny2025	0.011	0.018	-0.023	0.046	100	No
TRIG Graham2021	0.025	0.020	-0.014	0.063	100	No
VEGF Konieczny2025	-0.013	0.019	-0.051	0.024	100	No

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CI, confidence interval; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte

growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; SD, standard deviation; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor; VIP, variable inclusion probability. *Statistical significance at 95%CI

Table A13. Bootstrap results of the elastic-net penalized regression model predicting cardiovascular diseases within C10 of the multimodal stratification among the MDD sample of the UKB dataset.

Variable	Mean	SD	LowerCI	UpperCI	VIP	Significance
Area of caudalanteriorcingulate L	0.045	0.031	-0.017	0.105	100	No
Area of caudalanteriorcingulate R	-0.001	0.031	-0.062	0.060	100	No
Area of caudalmiddlefrontal L	0.001	0.029	-0.053	0.057	100	No
Area of caudalmiddlefrontal R	0.027	0.029	-0.029	0.085	100	No
Area of cuneus L	-0.030	0.030	-0.089	0.028	100	No
Area of cuneus R	-0.036	0.030	-0.092	0.023	100	No
Area of entorhinal L	0.014	0.032	-0.047	0.080	100	No
Area of entorhinal R	-0.007	0.031	-0.068	0.054	100	No
Area of fusiform L	-0.005	0.031	-0.063	0.055	100	No
Area of fusiform R	-0.043	0.031	-0.102	0.012	100	No
Area of inferiorparietal L	-0.035	0.029	-0.090	0.023	100	No
Area of inferiorparietal R	-0.008	0.029	-0.063	0.051	100	No
Area of inferiortemporal L	-0.034	0.029	-0.091	0.022	100	No
Area of inferiortemporal R	-0.023	0.029	-0.076	0.033	100	No
Area of insula L	-0.038	0.030	-0.097	0.019	100	No
Area of insula R	0.025	0.029	-0.033	0.082	100	No
Area of isthmuscingulate L	-0.010	0.030	-0.068	0.048	100	No
Area of isthmuscingulate R	0.043	0.032	-0.021	0.104	100	No
Area of lateraloccipital L	-0.011	0.029	-0.069	0.045	100	No
Area of lateraloccipital R	0.020	0.030	-0.038	0.082	100	No
Area of lateralorbitofrontal L	0.011	0.030	-0.047	0.068	100	No
Area of lateralorbitofrontal R	-0.010	0.030	-0.071	0.046	100	No
Area of lingual L	0.017	0.028	-0.039	0.071	100	No
Area of lingual R	-0.003	0.028	-0.059	0.051	100	No
Area of medialorbitofrontal L	-0.036	0.033	-0.103	0.029	100	No
Area of medialorbitofrontal R	-0.007	0.033	-0.071	0.056	100	No
Area of middletemporal L	-0.017	0.028	-0.073	0.037	100	No
Area of middletemporal R	0.004	0.028	-0.054	0.059	100	No
Area of paracentral L	0.009	0.033	-0.056	0.071	100	No
Area of paracentral R	-0.015	0.030	-0.076	0.044	100	No
Area of parahippocampal L	-0.016	0.033	-0.079	0.048	100	No
Area of parahippocampal R	0.009	0.033	-0.054	0.076	100	No
Area of parsopercularis L	-0.010	0.029	-0.066	0.048	100	No
Area of parsopercularis R	-0.011	0.030	-0.071	0.044	100	No
Area of parsorbitalis L	0.051	0.031	-0.011	0.106	100	No
Area of parsorbitalis R	0.001	0.031	-0.063	0.063	100	No
Area of parstriangularis L	-0.007	0.027	-0.066	0.048	100	No
Area of parstriangularis R	-0.013	0.029	-0.070	0.043	100	No
Area of pericalcarine L	-0.001	0.026	-0.050	0.048	100	No
Area of pericalcarine R	0.004	0.026	-0.048	0.053	100	No

Area of postcentral L	-0.013	0.031	-0.072	0.049	100	No
Area of postcentral R	0.019	0.031	-0.040	0.079	100	No
Area of posteriorcingulate L	-0.026	0.030	-0.086	0.030	100	No
Area of posteriorcingulate R	-0.012	0.030	-0.068	0.046	100	No
Area of precentral L	-0.014	0.030	-0.071	0.045	100	No
Area of precentral R	0.044	0.030	-0.014	0.105	100	No
Area of precuneus L	-0.009	0.029	-0.064	0.045	100	No
Area of precuneus R	-0.036	0.027	-0.087	0.020	100	No
Area of rostralanteriorcingulate L	0.043	0.030	-0.015	0.100	100	No
Area of rostralanteriorcingulate R	0.007	0.031	-0.057	0.069	100	No
Area of rostralmiddlefrontal L	0.006	0.030	-0.052	0.063	100	No
Area of rostralmiddlefrontal R	0.024	0.028	-0.030	0.079	100	No
Area of superiorfrontal L	-0.005	0.027	-0.056	0.051	100	No
Area of superiorfrontal R	-0.028	0.028	-0.078	0.027	100	No
Area of superiorparietal L	0.049	0.028	-0.006	0.107	100	No
Area of superiorparietal R	-0.017	0.029	-0.072	0.042	100	No
Area of superiortemporal L	-0.027	0.029	-0.085	0.027	100	No
Area of superiortemporal R	0.035	0.031	-0.025	0.093	100	No
Area of supramarginal L	0.002	0.030	-0.055	0.062	100	No
Area of supramarginal R	-0.004	0.029	-0.058	0.052	100	No
Area of transversetemporal L	0.012	0.031	-0.049	0.072	100	No
Area of transversetemporal R	0.067	0.033	0.002	0.132	100	Yes*
Mean thickness of caudalanteriorcingulate L	0.033	0.035	-0.038	0.100	100	No
Mean thickness of caudalanteriorcingulate R	0.024	0.034	-0.042	0.093	100	No
Mean thickness of caudalmiddlefrontal L	0.030	0.032	-0.031	0.093	100	No
Mean thickness of caudalmiddlefrontal R	-0.012	0.032	-0.073	0.050	100	No
Mean thickness of cuneus L	0.054	0.032	-0.008	0.117	100	No
Mean thickness of cuneus R	0.028	0.033	-0.035	0.091	100	No
Mean thickness of entorhinal L	-0.033	0.038	-0.103	0.039	100	No
Mean thickness of entorhinal R	0.007	0.037	-0.063	0.076	100	No
Mean thickness of fusiform L	0.000	0.035	-0.072	0.069	100	No
Mean thickness of fusiform R	-0.010	0.033	-0.076	0.052	100	No
Mean thickness of inferiorparietal L	-0.025	0.034	-0.088	0.042	100	No
Mean thickness of inferiorparietal R	0.000	0.031	-0.062	0.060	100	No
Mean thickness of inferiortemporal L	0.055	0.035	-0.016	0.129	100	No
Mean thickness of inferiortemporal R	-0.017	0.034	-0.087	0.051	100	No
Mean thickness of insula L	0.038	0.035	-0.026	0.107	100	No
Mean thickness of insula R	-0.075	0.034	-0.143	-0.011	100	Yes*
Mean thickness of isthmuscingulate L	0.043	0.037	-0.031	0.119	100	No
Mean thickness of isthmuscingulate R	-0.021	0.036	-0.092	0.049	100	No
Mean thickness of lateraloccipital L	0.030	0.032	-0.031	0.092	100	No
Mean thickness of lateraloccipital R	0.004	0.031	-0.059	0.064	100	No
Mean thickness of lateralorbitofrontal L	0.017	0.034	-0.051	0.086	100	No
Mean thickness of lateralorbitofrontal R	-0.003	0.032	-0.066	0.058	100	No

Mean thickness of lingual L	0.019	0.032	-0.042	0.080	100	No
Mean thickness of lingual R	0.048	0.032	-0.015	0.109	100	No
Mean thickness of medialorbitofrontal L	0.029	0.035	-0.041	0.095	100	No
Mean thickness of medialorbitofrontal R	0.018	0.034	-0.046	0.082	100	No
Mean thickness of middletemporal L	0.040	0.033	-0.025	0.107	100	No
Mean thickness of middletemporal R	-0.022	0.033	-0.091	0.041	100	No
Mean thickness of paracentral L	0.014	0.032	-0.045	0.074	100	No
Mean thickness of paracentral R	-0.022	0.032	-0.081	0.041	100	No
Mean thickness of parahippocampal L	-0.026	0.031	-0.088	0.036	100	No
Mean thickness of parahippocampal R	-0.045	0.034	-0.110	0.022	100	No
Mean thickness of parsopercularis L	0.008	0.037	-0.062	0.084	100	No
Mean thickness of parsopercularis R	-0.039	0.036	-0.105	0.031	100	No
Mean thickness of parsorbitalis L	-0.013	0.035	-0.080	0.053	100	No
Mean thickness of parsorbitalis R	-0.016	0.036	-0.094	0.052	100	No
Mean thickness of parstriangularis L	0.011	0.035	-0.056	0.078	100	No
Mean thickness of parstriangularis R	-0.017	0.035	-0.083	0.055	100	No
Mean thickness of pericalcarine L	0.001	0.035	-0.067	0.070	100	No
Mean thickness of pericalcarine R	0.039	0.034	-0.028	0.103	100	No
Mean thickness of postcentral L	0.017	0.030	-0.041	0.076	100	No
Mean thickness of postcentral R	0.014	0.031	-0.051	0.074	100	No
Mean thickness of posteriorcingulate L	0.005	0.035	-0.060	0.073	100	No
Mean thickness of posteriorcingulate R	-0.015	0.035	-0.080	0.053	100	No
Mean thickness of precentral L	-0.006	0.028	-0.061	0.050	100	No
Mean thickness of precentral R	-0.063	0.029	-0.120	-0.005	100	Yes*
Mean thickness of precuneus L	-0.009	0.032	-0.073	0.056	100	No
Mean thickness of precuneus R	-0.028	0.030	-0.087	0.031	100	No
Mean thickness of rostralanteriorcingulate L	-0.022	0.037	-0.093	0.049	100	No
Mean thickness of rostralanteriorcingulate R	-0.054	0.038	-0.126	0.022	100	No
Mean thickness of rostralmiddlefrontal L	0.001	0.033	-0.065	0.066	100	No
Mean thickness of rostralmiddlefrontal R	0.028	0.033	-0.031	0.093	100	No
Mean thickness of superiorfrontal L	-0.013	0.029	-0.072	0.043	100	No
Mean thickness of superiorfrontal R	-0.013	0.030	-0.073	0.047	100	No
Mean thickness of superiorparietal L	0.029	0.029	-0.027	0.087	100	No
Mean thickness of superiorparietal R	0.030	0.030	-0.028	0.088	100	No
Mean thickness of superiortemporal L	0.067	0.031	0.009	0.126	100	Yes*
Mean thickness of superiortemporal R	-0.001	0.031	-0.063	0.061	100	No
Mean thickness of supramarginal L	-0.048	0.034	-0.115	0.016	100	No
Mean thickness of supramarginal R	0.016	0.034	-0.045	0.093	100	No
Mean thickness of transversetemporal L	-0.010	0.035	-0.082	0.054	100	No
Mean thickness of transversetemporal R	-0.003	0.034	-0.072	0.064	100	No
Volume of caudalanteriorcingulate L	0.036	0.032	-0.029	0.096	100	No
Volume of caudalanteriorcingulate R	-0.011	0.029	-0.065	0.046	100	No
Volume of caudalmiddlefrontal L	0.022	0.030	-0.035	0.081	100	No
Volume of caudalmiddlefrontal R	0.020	0.029	-0.036	0.078	100	No

Volume of cuneus L	-0.002	0.028	-0.057	0.051	100	No
Volume of cuneus R	-0.008	0.027	-0.060	0.045	100	No
Volume of entorhinal L	0.007	0.033	-0.059	0.073	100	No
Volume of entorhinal R	0.018	0.034	-0.046	0.084	100	No
Volume of fusiform L	0.000	0.032	-0.066	0.060	100	No
Volume of fusiform R	-0.051	0.031	-0.113	0.005	100	No
Volume of inferiorparietal L	-0.045	0.029	-0.100	0.011	100	No
Volume of inferiorparietal R	-0.007	0.029	-0.066	0.050	100	No
Volume of inferiortemporal L	-0.023	0.030	-0.083	0.034	100	No
Volume of inferiortemporal R	-0.025	0.030	-0.083	0.033	100	No
Volume of insula L	-0.046	0.028	-0.099	0.010	100	No
Volume of insula R	-0.043	0.027	-0.095	0.011	100	No
Volume of isthmuscingulate L	-0.003	0.031	-0.060	0.060	100	No
Volume of isthmuscingulate R	0.035	0.031	-0.022	0.098	100	No
Volume of lateraloccipital L	-0.012	0.031	-0.075	0.049	100	No
Volume of lateraloccipital R	0.020	0.030	-0.036	0.081	100	No
Volume of lateralorbitofrontal L	0.007	0.030	-0.052	0.066	100	No
Volume of lateralorbitofrontal R	-0.015	0.032	-0.075	0.049	100	No
Volume of lingual L	0.020	0.027	-0.030	0.072	100	No
Volume of lingual R	0.029	0.027	-0.022	0.080	100	No
Volume of medialorbitofrontal L	-0.035	0.032	-0.101	0.026	100	No
Volume of medialorbitofrontal R	-0.016	0.032	-0.078	0.044	100	No
Volume of middletemporal L	-0.016	0.030	-0.077	0.043	100	No
Volume of middletemporal R	0.004	0.030	-0.056	0.063	100	No
Volume of paracentral L	0.032	0.031	-0.031	0.094	100	No
Volume of paracentral R	-0.009	0.031	-0.070	0.052	100	No
Volume of parahippocampal L	-0.023	0.027	-0.075	0.032	100	No
Volume of parahippocampal R	-0.023	0.030	-0.085	0.032	100	No
Volume of parsopercularis L	-0.004	0.030	-0.062	0.053	100	No
Volume of parsopercularis R	-0.041	0.030	-0.103	0.019	100	No
Volume of parsorbitalis L	0.022	0.032	-0.038	0.082	100	No
Volume of parsorbitalis R	0.029	0.032	-0.037	0.089	100	No
Volume of parstriangularis L	-0.012	0.029	-0.069	0.049	100	No
Volume of parstriangularis R	-0.030	0.030	-0.089	0.029	100	No
Volume of pericalcarine L	-0.003	0.026	-0.056	0.049	100	No
Volume of pericalcarine R	0.020	0.026	-0.031	0.068	100	No
Volume of postcentral L	-0.007	0.030	-0.063	0.054	100	No
Volume of postcentral R	0.021	0.029	-0.037	0.078	100	No
Volume of posterocingulate L	-0.025	0.030	-0.086	0.033	100	No
Volume of posterocingulate R	-0.023	0.031	-0.083	0.036	100	No
Volume of precentral L	-0.018	0.028	-0.071	0.036	100	No
Volume of precentral R	-0.006	0.028	-0.060	0.049	100	No
Volume of precuneus L	-0.005	0.029	-0.063	0.056	100	No
Volume of precuneus R	-0.060	0.027	-0.115	-0.007	100	Yes*

Volume of rostralanteriorcingulate L	0.012	0.032	-0.052	0.073	100	No
Volume of rostralanteriorcingulate R	-0.005	0.032	-0.066	0.058	100	No
Volume of rostralmiddlefrontal L	0.006	0.032	-0.053	0.065	100	No
Volume of rostralmiddlefrontal R	0.057	0.030	0.003	0.116	100	Yes*
Volume of superiorfrontal L	-0.004	0.029	-0.064	0.052	100	No
Volume of superiorfrontal R	-0.034	0.027	-0.087	0.022	100	No
Volume of superiorparietal L	0.067	0.030	0.009	0.128	100	Yes*
Volume of superiorparietal R	-0.002	0.029	-0.056	0.055	100	No
Volume of superiortemporal L	0.008	0.029	-0.051	0.062	100	No
Volume of superiortemporal R	0.044	0.030	-0.018	0.101	100	No
Volume of supramarginal L	-0.038	0.030	-0.099	0.021	100	No
Volume of supramarginal R	0.000	0.029	-0.052	0.057	100	No
Volume of transversetemporal L	-0.008	0.030	-0.069	0.051	100	No
Volume of transversetemporal R	0.032	0.033	-0.031	0.098	100	No
Volume of accumbens L	-0.007	0.038	-0.080	0.070	100	No
Volume of accumbens R	-0.016	0.038	-0.087	0.060	100	No
Volume of amygdala L	0.006	0.039	-0.073	0.087	100	No
Volume of amygdala R	0.010	0.038	-0.064	0.082	100	No
Volume of caudate L	0.003	0.034	-0.063	0.070	100	No
Volume of caudate R	-0.023	0.033	-0.086	0.038	100	No
Volume of hippocampus L	-0.039	0.039	-0.118	0.033	100	No
Volume of hippocampus R	0.013	0.036	-0.056	0.086	100	No
Volume of pallidum L	0.011	0.037	-0.061	0.083	100	No
Volume of pallidum R	0.019	0.036	-0.050	0.089	100	No
Volume of putamen L	-0.004	0.034	-0.070	0.061	100	No
Volume of putamen R	-0.004	0.033	-0.065	0.056	100	No
Volume of thalamus L	-0.013	0.030	-0.071	0.047	100	No
Volume of thalamus R	0.003	0.030	-0.054	0.059	100	No
Mean FA in anterior corona radiata L	-0.039	0.027	-0.092	0.013	100	No
Mean FA in anterior corona radiata R	0.010	0.028	-0.044	0.064	100	No
Mean FA in anterior limb of internal capsule L	0.017	0.028	-0.039	0.073	100	No
Mean FA in anterior limb of internal capsule R	-0.004	0.028	-0.058	0.050	100	No
Mean FA in body of corpus callosum	-0.020	0.028	-0.077	0.036	100	No
Mean FA in cerebral peduncle L	0.029	0.026	-0.023	0.079	100	No
Mean FA in cerebral peduncle R	0.016	0.027	-0.036	0.071	100	No
Mean FA in cingulum cingulate gyrus L	-0.013	0.027	-0.062	0.042	100	No
Mean FA in cingulum cingulate gyrus R	-0.005	0.026	-0.059	0.044	100	No
Mean FA in cingulum hippocampus L	0.016	0.028	-0.041	0.068	100	No
Mean FA in cingulum hippocampus R	-0.005	0.029	-0.059	0.052	100	No
Mean FA in corticospinal tract L	-0.001	0.033	-0.064	0.063	100	No
Mean FA in corticospinal tract R	0.010	0.032	-0.048	0.072	100	No
Mean FA in external capsule L	0.006	0.026	-0.045	0.057	100	No
Mean FA in external capsule R	-0.012	0.029	-0.068	0.043	100	No
Mean FA in fornix cres+stria terminalis L	-0.024	0.028	-0.078	0.035	100	No

Mean FA in fornix cres+stria terminalis R	0.026	0.030	-0.034	0.086	100	No
Mean FA in fornix	-0.006	0.029	-0.067	0.049	100	No
Mean FA in genu of corpus callosum	-0.017	0.027	-0.070	0.035	100	No
Mean FA in inferior cerebellar peduncle L	-0.009	0.027	-0.063	0.046	100	No
Mean FA in inferior cerebellar peduncle R	0.004	0.027	-0.048	0.056	100	No
Mean FA in medial lemniscus L	0.003	0.029	-0.049	0.058	100	No
Mean FA in medial lemniscus R	-0.005	0.030	-0.062	0.052	100	No
Mean FA in middle cerebellar peduncle	0.008	0.032	-0.054	0.070	100	No
Mean FA in pontine crossing tract	0.001	0.035	-0.064	0.072	100	No
Mean FA in posterior corona radiata L	0.037	0.029	-0.022	0.092	100	No
Mean FA in posterior corona radiata R	0.032	0.027	-0.020	0.087	100	No
Mean FA in posterior limb of internal capsule L	0.015	0.025	-0.034	0.066	100	No
Mean FA in posterior limb of internal capsule R	0.000	0.025	-0.046	0.046	100	No
Mean FA in posterior thalamic radiation L	-0.031	0.028	-0.088	0.022	100	No
Mean FA in posterior thalamic radiation R	-0.022	0.029	-0.079	0.038	100	No
Mean FA in retrolenticular part of internal capsule L	-0.057	0.028	-0.110	-0.002	100	Yes*
Mean FA in retrolenticular part of internal capsule R	0.023	0.027	-0.030	0.071	100	No
Mean FA in sagittal stratum L	-0.015	0.028	-0.072	0.038	100	No
Mean FA in sagittal stratum R	0.051	0.028	-0.003	0.105	100	No
Mean FA in splenium of corpus callosum	0.015	0.028	-0.039	0.065	100	No
Mean FA in superior cerebellar peduncle L	0.007	0.026	-0.046	0.057	100	No
Mean FA in superior cerebellar peduncle R	0.006	0.026	-0.046	0.055	100	No
Mean FA in superior corona radiata L	-0.007	0.027	-0.057	0.047	100	No
Mean FA in superior corona radiata R	0.019	0.028	-0.037	0.074	100	No
Mean FA in superior fronto-occipital fasciculus L	-0.047	0.029	-0.103	0.008	100	No
Mean FA in superior fronto-occipital fasciculus R	-0.030	0.030	-0.086	0.029	100	No
Mean FA in superior longitudinal fasciculus L	-0.005	0.027	-0.057	0.048	100	No
Mean FA in superior longitudinal fasciculus R	0.019	0.027	-0.031	0.073	100	No
Mean FA in tapetum L	0.002	0.031	-0.056	0.063	100	No
Mean FA in tapetum R	0.026	0.033	-0.037	0.094	100	No
Mean FA in uncinate fasciculus L	-0.022	0.030	-0.080	0.038	100	No
Mean FA in uncinate fasciculus R	-0.029	0.028	-0.088	0.025	100	No
Mean L1 in anterior corona radiata L	-0.041	0.031	-0.103	0.018	100	No
Mean L1 in anterior corona radiata R	-0.008	0.029	-0.064	0.049	100	No
Mean L1 in anterior limb of internal capsule L	0.004	0.032	-0.055	0.069	100	No
Mean L1 in anterior limb of internal capsule R	-0.007	0.033	-0.074	0.052	100	No
Mean L1 in body of corpus callosum	0.001	0.033	-0.063	0.067	100	No
Mean L1 in cerebral peduncle L	-0.068	0.035	-0.134	-0.001	100	Yes*
Mean L1 in cerebral peduncle R	-0.056	0.033	-0.117	0.010	100	No
Mean L1 in cingulum cingulate gyrus L	-0.006	0.032	-0.068	0.055	100	No
Mean L1 in cingulum cingulate gyrus R	0.010	0.031	-0.049	0.072	100	No
Mean L1 in cingulum hippocampus L	0.024	0.034	-0.046	0.088	100	No
Mean L1 in cingulum hippocampus R	-0.038	0.033	-0.101	0.026	100	No
Mean L1 in corticospinal tract L	-0.009	0.032	-0.068	0.052	100	No

Mean L1 in corticospinal tract R	-0.024	0.030	-0.084	0.034	100	No
Mean L1 in external capsule L	0.083	0.030	0.025	0.139	100	Yes*
Mean L1 in external capsule R	0.072	0.031	0.011	0.130	100	Yes*
Mean L1 in fornix cres+stria terminalis L	0.017	0.033	-0.046	0.084	100	No
Mean L1 in fornix cres+stria terminalis R	0.052	0.034	-0.015	0.115	100	No
Mean L1 in fornix	-0.025	0.029	-0.079	0.036	100	No
Mean L1 in genu of corpus callosum	-0.032	0.034	-0.101	0.032	100	No
Mean L1 in inferior cerebellar peduncle L	0.006	0.032	-0.059	0.069	100	No
Mean L1 in inferior cerebellar peduncle R	-0.052	0.032	-0.115	0.010	100	No
Mean L1 in medial lemniscus L	-0.017	0.029	-0.075	0.038	100	No
Mean L1 in medial lemniscus R	-0.017	0.028	-0.070	0.037	100	No
Mean L1 in middle cerebellar peduncle	0.015	0.030	-0.046	0.071	100	No
Mean L1 in pontine crossing tract	-0.033	0.026	-0.086	0.016	100	No
Mean L1 in posterior corona radiata L	-0.020	0.029	-0.078	0.042	100	No
Mean L1 in posterior corona radiata R	-0.053	0.030	-0.113	0.006	100	No
Mean L1 in posterior limb of internal capsule L	-0.001	0.032	-0.064	0.058	100	No
Mean L1 in posterior limb of internal capsule R	-0.026	0.030	-0.083	0.031	100	No
Mean L1 in posterior thalamic radiation L	0.029	0.032	-0.032	0.092	100	No
Mean L1 in posterior thalamic radiation R	-0.035	0.032	-0.096	0.029	100	No
Mean L1 in retrolenticular part of internal capsule L	-0.038	0.033	-0.103	0.027	100	No
Mean L1 in retrolenticular part of internal capsule R	-0.035	0.033	-0.099	0.029	100	No
Mean L1 in sagittal stratum L	-0.033	0.031	-0.098	0.024	100	No
Mean L1 in sagittal stratum R	0.016	0.032	-0.046	0.076	100	No
Mean L1 in splenium of corpus callosum	0.008	0.034	-0.060	0.071	100	No
Mean L1 in superior cerebellar peduncle L	-0.002	0.031	-0.062	0.060	100	No
Mean L1 in superior cerebellar peduncle R	0.013	0.029	-0.046	0.068	100	No
Mean L1 in superior corona radiata L	0.007	0.028	-0.045	0.062	100	No
Mean L1 in superior corona radiata R	-0.033	0.027	-0.087	0.018	100	No
Mean L1 in superior fronto-occipital fasciculus L	0.024	0.035	-0.047	0.089	100	No
Mean L1 in superior fronto-occipital fasciculus R	-0.043	0.034	-0.112	0.025	100	No
Mean L1 in superior longitudinal fasciculus L	0.031	0.031	-0.031	0.091	100	No
Mean L1 in superior longitudinal fasciculus R	0.010	0.029	-0.050	0.067	100	No
Mean L1 in tapetum L	0.014	0.035	-0.058	0.085	100	No
Mean L1 in tapetum R	0.031	0.037	-0.046	0.100	100	No
Mean L1 in uncinate fasciculus L	0.005	0.034	-0.060	0.069	100	No
Mean L1 in uncinate fasciculus R	0.000	0.035	-0.067	0.066	100	No
Mean RD in anterior corona radiata L	0.015	0.025	-0.035	0.065	100	No
Mean RD in anterior corona radiata R	-0.014	0.024	-0.062	0.031	100	No
Mean RD in anterior limb of internal capsule L	0.005	0.028	-0.050	0.058	100	No
Mean RD in anterior limb of internal capsule R	0.012	0.028	-0.041	0.065	100	No
Mean RD in body of corpus callosum	0.008	0.029	-0.046	0.065	100	No
Mean RD in cerebral peduncle L	-0.036	0.028	-0.090	0.020	100	No
Mean RD in cerebral peduncle R	-0.021	0.028	-0.073	0.032	100	No
Mean RD in cingulum cingulate gyrus L	0.015	0.028	-0.041	0.070	100	No

Mean RD in cingulum cingulate gyrus R	0.017	0.027	-0.034	0.073	100	No
Mean RD in cingulum hippocampus L	-0.011	0.029	-0.067	0.046	100	No
Mean RD in cingulum hippocampus R	-0.007	0.031	-0.065	0.055	100	No
Mean RD in corticospinal tract L	-0.003	0.026	-0.051	0.051	100	No
Mean RD in corticospinal tract R	-0.026	0.024	-0.073	0.024	100	No
Mean RD in external capsule L	0.049	0.026	-0.005	0.099	100	No
Mean RD in external capsule R	0.046	0.027	-0.006	0.102	100	No
Mean RD in fornix cres+stria terminalis L	0.023	0.028	-0.033	0.077	100	No
Mean RD in fornix cres+stria terminalis R	0.009	0.029	-0.047	0.063	100	No
Mean RD in fornix	-0.012	0.024	-0.054	0.036	100	No
Mean RD in genu of corpus callosum	0.001	0.027	-0.053	0.052	100	No
Mean RD in inferior cerebellar peduncle L	0.015	0.030	-0.040	0.076	100	No
Mean RD in inferior cerebellar peduncle R	-0.027	0.030	-0.087	0.033	100	No
Mean RD in medial lemniscus L	-0.016	0.023	-0.063	0.030	100	No
Mean RD in medial lemniscus R	-0.009	0.024	-0.057	0.039	100	No
Mean RD in middle cerebellar peduncle	0.010	0.028	-0.045	0.064	100	No
Mean RD in pontine crossing tract	-0.029	0.023	-0.073	0.016	100	No
Mean RD in posterior corona radiata L	-0.043	0.025	-0.092	0.005	100	No
Mean RD in posterior corona radiata R	-0.051	0.025	-0.100	-0.003	100	Yes*
Mean RD in posterior limb of internal capsule L	-0.006	0.028	-0.060	0.051	100	No
Mean RD in posterior limb of internal capsule R	-0.003	0.028	-0.058	0.049	100	No
Mean RD in posterior thalamic radiation L	0.051	0.024	0.000	0.099	100	No
Mean RD in posterior thalamic radiation R	0.004	0.026	-0.048	0.056	100	No
Mean RD in retrolenticular part of internal capsule L	0.050	0.029	-0.007	0.107	100	No
Mean RD in retrolenticular part of internal capsule R	-0.032	0.028	-0.085	0.026	100	No
Mean RD in sagittal stratum L	-0.003	0.028	-0.056	0.055	100	No
Mean RD in sagittal stratum R	-0.042	0.027	-0.096	0.007	100	No
Mean RD in splenium of corpus callosum	-0.009	0.029	-0.061	0.050	100	No
Mean RD in superior cerebellar peduncle L	0.000	0.026	-0.051	0.050	100	No
Mean RD in superior cerebellar peduncle R	0.015	0.027	-0.036	0.068	100	No
Mean RD in superior corona radiata L	0.026	0.025	-0.024	0.076	100	No
Mean RD in superior corona radiata R	-0.027	0.024	-0.072	0.018	100	No
Mean RD in superior fronto-occipital fasciculus L	0.054	0.030	-0.004	0.110	100	No
Mean RD in superior fronto-occipital fasciculus R	-0.007	0.030	-0.066	0.053	100	No
Mean RD in superior longitudinal fasciculus L	0.007	0.027	-0.043	0.058	100	No
Mean RD in superior longitudinal fasciculus R	-0.020	0.026	-0.072	0.028	100	No
Mean RD in tapetum L	0.005	0.027	-0.045	0.057	100	No
Mean RD in tapetum R	-0.007	0.028	-0.061	0.046	100	No
Mean RD in uncinate fasciculus L	0.034	0.030	-0.029	0.090	100	No
Mean RD in uncinate fasciculus R	0.027	0.029	-0.028	0.087	100	No
Spos_1	-0.029	0.036	-0.099	0.040	100	No
Spos_2	-0.008	0.037	-0.083	0.060	100	No
Spos_3	-0.034	0.035	-0.101	0.034	100	No
Spos_4	-0.001	0.037	-0.072	0.069	100	No

Spos_5	0.008	0.039	-0.074	0.083	100	No
Spos_6	0.010	0.039	-0.065	0.086	100	No
Spos_7	-0.010	0.039	-0.088	0.066	100	No
Spos_8	-0.011	0.037	-0.086	0.071	100	No
Spos_9	0.042	0.039	-0.037	0.121	100	No
Spos_10	-0.040	0.040	-0.118	0.037	100	No
Spos_11	-0.036	0.039	-0.118	0.044	100	No
Spos_12	0.001	0.042	-0.079	0.081	100	No
Spos_13	-0.050	0.037	-0.120	0.022	100	No
Spos_14	0.069	0.038	-0.005	0.144	100	No
Spos_15	0.010	0.038	-0.066	0.082	100	No
Spos_16	-0.020	0.035	-0.088	0.046	100	No
Spos_17	-0.048	0.039	-0.123	0.029	100	No
Spos_18	-0.017	0.041	-0.089	0.062	100	No
Spos_19	-0.016	0.042	-0.096	0.066	100	No
Spos_20	0.004	0.039	-0.072	0.079	100	No
Spos_21	0.014	0.038	-0.060	0.086	100	No
Spos_22	-0.046	0.039	-0.123	0.032	100	No
Spos_23	-0.051	0.040	-0.130	0.026	100	No
Spos_24	-0.016	0.040	-0.098	0.061	100	No
Spos_25	-0.018	0.039	-0.098	0.057	100	No
Spos_26	0.033	0.040	-0.044	0.114	100	No
Spos_27	-0.055	0.037	-0.130	0.017	100	No
Spos_28	-0.042	0.039	-0.114	0.035	100	No
Spos_29	0.002	0.041	-0.076	0.084	100	No
Spos_30	-0.007	0.037	-0.081	0.066	100	No
Spos_31	-0.020	0.040	-0.099	0.055	100	No
Spos_32	0.018	0.039	-0.057	0.095	100	No
Spos_33	0.010	0.040	-0.067	0.091	100	No
Spos_34	0.048	0.038	-0.030	0.120	100	No
Spos_35	-0.034	0.040	-0.112	0.037	100	No
Spos_36	0.009	0.042	-0.072	0.095	100	No
Spos_37	-0.013	0.038	-0.081	0.065	100	No
Spos_38	0.032	0.037	-0.038	0.108	100	No
Spos_39	-0.061	0.039	-0.136	0.016	100	No
Spos_40	-0.096	0.038	-0.168	-0.020	100	Yes*
Spos_41	-0.016	0.037	-0.086	0.057	100	No
Spos_42	0.033	0.038	-0.038	0.107	100	No
Spos_43	-0.003	0.040	-0.081	0.074	100	No
Spos_44	-0.047	0.038	-0.121	0.031	100	No
Spos_45	0.007	0.037	-0.062	0.081	100	No
Spos_46	0.025	0.041	-0.056	0.102	100	No
Spos_47	-0.006	0.036	-0.074	0.066	100	No
Spos_48	-0.030	0.039	-0.109	0.045	100	No

Spos_49	0.042	0.038	-0.029	0.118	100	No
Spos_50	0.072	0.040	-0.005	0.150	100	No
Spos_51	-0.001	0.040	-0.072	0.080	100	No
Spos_52	-0.013	0.039	-0.087	0.060	100	No
Spos_53	0.047	0.041	-0.035	0.125	100	No
Spos_54	0.000	0.040	-0.080	0.078	100	No
Spos_55	0.038	0.039	-0.041	0.117	100	No
Sneg_1	0.037	0.036	-0.030	0.107	100	No
Sneg_2	-0.018	0.039	-0.091	0.053	100	No
Sneg_3	-0.002	0.038	-0.073	0.072	100	No
Sneg_4	-0.001	0.036	-0.069	0.069	100	No
Sneg_5	-0.002	0.040	-0.078	0.076	100	No
Sneg_6	0.018	0.039	-0.062	0.091	100	No
Sneg_7	-0.030	0.039	-0.107	0.049	100	No
Sneg_8	-0.019	0.035	-0.091	0.049	100	No
Sneg_9	-0.070	0.040	-0.146	0.012	100	No
Sneg_10	-0.044	0.042	-0.121	0.041	100	No
Sneg_11	-0.017	0.041	-0.097	0.065	100	No
Sneg_12	-0.036	0.040	-0.115	0.040	100	No
Sneg_13	0.045	0.040	-0.038	0.120	100	No
Sneg_14	-0.060	0.036	-0.132	0.013	100	No
Sneg_15	0.048	0.039	-0.028	0.124	100	No
Sneg_16	-0.039	0.033	-0.103	0.028	100	No
Sneg_17	-0.028	0.042	-0.111	0.053	100	No
Sneg_18	-0.013	0.042	-0.097	0.069	100	No
Sneg_19	0.022	0.041	-0.060	0.101	100	No
Sneg_20	0.047	0.040	-0.030	0.124	100	No
Sneg_21	-0.057	0.041	-0.135	0.023	100	No
Sneg_22	0.034	0.040	-0.046	0.112	100	No
Sneg_23	-0.021	0.040	-0.096	0.053	100	No
Sneg_24	0.009	0.041	-0.073	0.087	100	No
Sneg_25	-0.002	0.039	-0.076	0.079	100	No
Sneg_26	0.081	0.042	0.000	0.160	100	No
Sneg_27	-0.020	0.040	-0.101	0.057	100	No
Sneg_28	-0.011	0.039	-0.084	0.073	100	No
Sneg_29	-0.002	0.039	-0.076	0.072	100	No
Sneg_30	-0.067	0.039	-0.144	0.006	100	No
Sneg_31	0.041	0.038	-0.033	0.114	100	No
Sneg_32	0.028	0.038	-0.046	0.099	100	No
Sneg_33	0.093	0.039	0.017	0.169	100	Yes*
Sneg_34	0.009	0.039	-0.071	0.086	100	No
Sneg_35	-0.048	0.039	-0.125	0.031	100	No
Sneg_36	-0.009	0.040	-0.084	0.073	100	No
Sneg_37	0.017	0.038	-0.057	0.090	100	No

Sneg_38	-0.026	0.041	-0.109	0.058	100	No
Sneg_39	0.028	0.038	-0.048	0.101	100	No
Sneg_40	0.027	0.041	-0.056	0.107	100	No
Sneg_41	-0.005	0.037	-0.080	0.062	100	No
Sneg_42	-0.006	0.038	-0.083	0.068	100	No
Sneg_43	0.000	0.040	-0.079	0.075	100	No
Sneg_44	0.003	0.040	-0.073	0.083	100	No
Sneg_45	-0.034	0.039	-0.114	0.043	100	No
Sneg_46	-0.040	0.041	-0.120	0.036	100	No
Sneg_47	0.009	0.038	-0.059	0.088	100	No
Sneg_48	-0.044	0.039	-0.119	0.034	100	No
Sneg_49	0.008	0.039	-0.068	0.085	100	No
Sneg_50	-0.046	0.039	-0.121	0.031	100	No
Sneg_51	0.012	0.040	-0.064	0.089	100	No
Sneg_52	0.031	0.040	-0.050	0.103	100	No
Sneg_53	0.016	0.041	-0.062	0.092	100	No
Sneg_54	-0.052	0.041	-0.131	0.033	100	No
Sneg_55	0.064	0.038	-0.008	0.139	100	No
Median z-statistic (amygdala) for faces-shapes contrast	-0.012	0.031	-0.074	0.049	100	No
Median z-statistic for faces activation	-0.006	0.024	-0.051	0.042	100	No
Median z-statistic for shapes activation	-0.004	0.026	-0.055	0.048	100	No
Median z-statistic for faces-shapes contrast	0.009	0.031	-0.054	0.072	100	No
90th percentile of z-statistic (amygdala) for faces-shapes contrast	-0.020	0.032	-0.081	0.041	100	No
90th percentile of z-statistic for faces activation	-0.012	0.021	-0.053	0.032	100	No
90th percentile of z-statistic for shapes activation	-0.012	0.024	-0.057	0.039	100	No
90th percentile of z-statistic for faces-shapes contrast	0.001	0.028	-0.057	0.054	100	No
ALCDEP Walters2018	0.011	0.042	-0.068	0.100	100	No
AN Watson2019	-0.012	0.043	-0.093	0.071	100	No
ASD Grove2019	-0.015	0.042	-0.098	0.066	100	No
BD PGC4 2025	-0.014	0.040	-0.094	0.067	100	No
BMI Locke2015	0.047	0.040	-0.027	0.125	100	No
Bngf Konieczny2025	-0.037	0.041	-0.118	0.045	100	No
CAD Nikpay2015	0.052	0.042	-0.035	0.132	100	No
CCL11 Konieczny2025	-0.049	0.042	-0.135	0.033	100	No
CCL2 Konieczny2025	-0.002	0.041	-0.082	0.080	100	No
CCL3 Konieczny2025	0.046	0.043	-0.038	0.132	100	No
CCL4 Konieczny2025	-0.038	0.042	-0.123	0.045	100	No
CCL7 MCP3 Konieczny2025	-0.025	0.043	-0.104	0.062	100	No
CRP Said2022	0.027	0.041	-0.054	0.107	100	No
CSF1 Konieczny2025	-0.020	0.043	-0.105	0.064	100	No
CSF3 Konieczny2025	0.030	0.041	-0.053	0.106	100	No
CTACK Konieczny2025	0.002	0.038	-0.070	0.072	100	No
CUD Johnson2020	0.027	0.041	-0.054	0.109	100	No
CXCL1 Konieczny2025	0.045	0.040	-0.036	0.122	100	No

CXCL10 Konieczny2025	0.010	0.039	-0.060	0.087	100	No
CXCL12 Konieczny2025	0.008	0.040	-0.070	0.087	100	No
CXCL9 Konieczny2025	-0.005	0.039	-0.081	0.070	100	No
FGFb Konieczny2025	-0.013	0.042	-0.092	0.071	100	No
GAD FinnGen2024	0.025	0.041	-0.058	0.105	100	No
HbA1c Willems2023	0.005	0.040	-0.072	0.083	100	No
HDL Graham2021	0.027	0.037	-0.043	0.102	100	No
HGF Konieczny2025	0.013	0.040	-0.066	0.090	100	No
IFNg Konieczny2025	-0.012	0.033	-0.078	0.052	100	No
IL10 Konieczny2025	0.008	0.037	-0.067	0.082	100	No
IL13 Konieczny2025	-0.032	0.029	-0.090	0.026	100	No
IL16 Konieczny2025	0.004	0.044	-0.080	0.086	100	No
IL17 Konieczny2025	-0.019	0.034	-0.085	0.050	100	No
IL18 Konieczny2025	-0.041	0.042	-0.123	0.040	100	No
IL1b Konieczny2025	-0.032	0.041	-0.112	0.048	100	No
IL1RA Konieczny2025	0.038	0.041	-0.042	0.119	100	No
IL2 Konieczny2025	0.045	0.041	-0.035	0.125	100	No
IL2RA Konieczny2025	-0.018	0.043	-0.098	0.065	100	No
IL4 Konieczny2025	-0.010	0.031	-0.071	0.059	100	No
IL5 Konieczny2025	0.002	0.036	-0.070	0.070	100	No
IL6 Konieczny2025	-0.025	0.040	-0.107	0.057	100	No
IL7 Konieczny2025	-0.039	0.032	-0.102	0.025	100	No
IL8 Konieczny2025	0.018	0.038	-0.055	0.092	100	No
IL9 Konieczny2025	-0.014	0.039	-0.087	0.066	100	No
LDL Graham2021	-0.043	0.042	-0.128	0.040	100	No
MDD PGC4_2025	0.008	0.038	-0.063	0.083	100	No
MIF Konieczny2025	-0.015	0.042	-0.095	0.070	100	No
NEUROT DeMoor2015	0.047	0.043	-0.036	0.129	100	No
OCD PGC3 2018	0.034	0.043	-0.055	0.116	100	No
PDGFbB Konieczny2025	-0.020	0.040	-0.095	0.059	100	No
PTSD Nievergelt2024	0.009	0.040	-0.069	0.092	100	No
RANTES Konieczny2025	0.000	0.041	-0.075	0.079	100	No
SCF Konieczny2025	-0.001	0.042	-0.079	0.085	100	No
SCGFb Konieczny2025	0.020	0.041	-0.061	0.098	100	No
SCZ Trubetskoy2022	-0.025	0.042	-0.103	0.064	100	No
T2D Verma2024	0.115	0.041	0.033	0.194	100	Yes*
TNFa Konieczny2025	0.052	0.032	-0.013	0.115	100	No
TNFb Konieczny2025	0.021	0.031	-0.040	0.084	100	No
TRAIL Konieczny2025	-0.035	0.041	-0.112	0.044	100	No
TRIG Graham2021	0.057	0.038	-0.014	0.133	100	No
VEGF Konieczny2025	-0.037	0.039	-0.110	0.041	100	No

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CI, confidence interval; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder;

*FA, fractional anisotropy; FGFb, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; SD, standard deviation; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor; VIP, variable inclusion probability. *Statistical significance at 95%CI*

Table A14. Bootstrap results of the elastic-net penalized regression model predicting cardiovascular diseases within C11 of the multimodal stratification among the MDD sample of the UKB dataset.

Variable	Mean	SD	LowerCI	UpperCI	VIP	Significance
Area of caudalanteriorcingulate L	0.013	0.029	-0.044	0.069	100	No
Area of caudalanteriorcingulate R	-0.017	0.030	-0.073	0.042	100	No
Area of caudalmiddlefrontal L	-0.002	0.030	-0.059	0.056	100	No
Area of caudalmiddlefrontal R	0.008	0.028	-0.050	0.064	100	No
Area of cuneus L	-0.024	0.031	-0.084	0.038	100	No
Area of cuneus R	-0.032	0.031	-0.089	0.031	100	No
Area of entorhinal L	0.039	0.032	-0.025	0.103	100	No
Area of entorhinal R	0.026	0.033	-0.039	0.089	100	No
Area of fusiform L	-0.002	0.029	-0.060	0.054	100	No
Area of fusiform R	0.023	0.030	-0.037	0.082	100	No
Area of inferiorparietal L	-0.019	0.030	-0.078	0.039	100	No
Area of inferiorparietal R	-0.003	0.031	-0.064	0.057	100	No
Area of inferiortemporal L	-0.057	0.028	-0.111	-0.001	100	Yes*
Area of inferiortemporal R	-0.003	0.030	-0.061	0.056	100	No
Area of insula L	0.035	0.030	-0.025	0.092	100	No
Area of insula R	0.022	0.031	-0.038	0.080	100	No
Area of isthmuscingulate L	0.023	0.031	-0.037	0.086	100	No
Area of isthmuscingulate R	0.011	0.031	-0.049	0.075	100	No
Area of lateraloccipital L	-0.015	0.030	-0.071	0.043	100	No
Area of lateraloccipital R	0.018	0.031	-0.043	0.077	100	No
Area of lateralorbitofrontal L	-0.041	0.031	-0.099	0.019	100	No
Area of lateralorbitofrontal R	0.026	0.031	-0.034	0.084	100	No
Area of lingual L	-0.028	0.030	-0.093	0.031	100	No
Area of lingual R	0.016	0.029	-0.043	0.073	100	No
Area of medialorbitofrontal L	-0.018	0.034	-0.085	0.047	100	No
Area of medialorbitofrontal R	-0.009	0.034	-0.071	0.057	100	No
Area of middletemporal L	0.027	0.028	-0.024	0.082	100	No
Area of middletemporal R	-0.073	0.029	-0.129	-0.015	100	Yes*
Area of paracentral L	0.062	0.031	0.002	0.123	100	Yes*
Area of paracentral R	-0.008	0.031	-0.072	0.053	100	No
Area of parahippocampal L	-0.032	0.036	-0.101	0.042	100	No
Area of parahippocampal R	0.017	0.036	-0.053	0.089	100	No
Area of parsopercularis L	-0.036	0.030	-0.095	0.023	100	No
Area of parsopercularis R	-0.018	0.028	-0.072	0.034	100	No
Area of parsorbitalis L	-0.019	0.032	-0.083	0.047	100	No
Area of parsorbitalis R	-0.019	0.032	-0.085	0.045	100	No
Area of parstriangularis L	-0.034	0.028	-0.088	0.020	100	No
Area of parstriangularis R	-0.008	0.030	-0.065	0.049	100	No
Area of pericalcarine L	-0.028	0.028	-0.083	0.026	100	No
Area of pericalcarine R	0.022	0.026	-0.030	0.071	100	No

Area of postcentral L	0.000	0.032	-0.062	0.058	100	No
Area of postcentral R	-0.018	0.031	-0.079	0.040	100	No
Area of posteriorcingulate L	-0.018	0.029	-0.075	0.040	100	No
Area of posteriorcingulate R	-0.012	0.030	-0.070	0.049	100	No
Area of precentral L	-0.034	0.032	-0.091	0.031	100	No
Area of precentral R	0.002	0.030	-0.055	0.061	100	No
Area of precuneus L	0.022	0.029	-0.038	0.076	100	No
Area of precuneus R	0.000	0.028	-0.054	0.054	100	No
Area of rostralanteriorcingulate L	-0.002	0.030	-0.060	0.057	100	No
Area of rostralanteriorcingulate R	0.007	0.031	-0.053	0.070	100	No
Area of rostralmiddlefrontal L	-0.032	0.029	-0.088	0.025	100	No
Area of rostralmiddlefrontal R	-0.003	0.028	-0.057	0.054	100	No
Area of superiorfrontal L	-0.004	0.029	-0.067	0.053	100	No
Area of superiorfrontal R	-0.031	0.028	-0.088	0.023	100	No
Area of superiorparietal L	0.043	0.029	-0.017	0.098	100	No
Area of superiorparietal R	0.037	0.029	-0.023	0.096	100	No
Area of superiortemporal L	0.018	0.030	-0.043	0.077	100	No
Area of superiortemporal R	-0.006	0.031	-0.064	0.054	100	No
Area of supramarginal L	-0.017	0.029	-0.076	0.040	100	No
Area of supramarginal R	-0.021	0.030	-0.077	0.039	100	No
Area of transversetemporal L	0.039	0.031	-0.025	0.099	100	No
Area of transversetemporal R	-0.001	0.034	-0.066	0.066	100	No
Mean thickness of caudalanteriorcingulate L	-0.015	0.035	-0.080	0.056	100	No
Mean thickness of caudalanteriorcingulate R	0.013	0.035	-0.055	0.079	100	No
Mean thickness of caudalmiddlefrontal L	0.049	0.033	-0.011	0.113	100	No
Mean thickness of caudalmiddlefrontal R	0.022	0.033	-0.039	0.085	100	No
Mean thickness of cuneus L	0.027	0.033	-0.036	0.091	100	No
Mean thickness of cuneus R	0.069	0.032	0.006	0.132	100	Yes*
Mean thickness of entorhinal L	-0.039	0.037	-0.106	0.035	100	No
Mean thickness of entorhinal R	0.042	0.037	-0.031	0.111	100	No
Mean thickness of fusiform L	-0.015	0.035	-0.080	0.051	100	No
Mean thickness of fusiform R	-0.041	0.032	-0.106	0.020	100	No
Mean thickness of inferiorparietal L	-0.024	0.032	-0.085	0.040	100	No
Mean thickness of inferiorparietal R	-0.008	0.031	-0.065	0.054	100	No
Mean thickness of inferiortemporal L	-0.062	0.034	-0.129	0.010	100	No
Mean thickness of inferiortemporal R	0.004	0.034	-0.064	0.070	100	No
Mean thickness of insula L	-0.014	0.032	-0.077	0.047	100	No
Mean thickness of insula R	-0.030	0.033	-0.093	0.032	100	No
Mean thickness of isthmuscingulate L	-0.067	0.035	-0.137	0.001	100	No
Mean thickness of isthmuscingulate R	-0.031	0.038	-0.103	0.043	100	No
Mean thickness of lateraloccipital L	0.041	0.031	-0.017	0.099	100	No
Mean thickness of lateraloccipital R	-0.013	0.031	-0.073	0.049	100	No
Mean thickness of lateralorbitofrontal L	0.022	0.033	-0.042	0.086	100	No
Mean thickness of lateralorbitofrontal R	-0.007	0.034	-0.072	0.057	100	No

Mean thickness of lingual L	0.013	0.031	-0.051	0.077	100	No
Mean thickness of lingual R	0.012	0.031	-0.048	0.072	100	No
Mean thickness of medialorbitofrontal L	0.006	0.036	-0.066	0.077	100	No
Mean thickness of medialorbitofrontal R	0.071	0.036	0.002	0.142	100	Yes*
Mean thickness of middletemporal L	-0.023	0.032	-0.085	0.041	100	No
Mean thickness of middletemporal R	0.046	0.031	-0.013	0.106	100	No
Mean thickness of paracentral L	-0.037	0.030	-0.095	0.020	100	No
Mean thickness of paracentral R	-0.030	0.031	-0.090	0.027	100	No
Mean thickness of parahippocampal L	0.010	0.033	-0.053	0.078	100	No
Mean thickness of parahippocampal R	-0.013	0.032	-0.075	0.044	100	No
Mean thickness of parsopercularis L	0.019	0.034	-0.046	0.084	100	No
Mean thickness of parsopercularis R	-0.009	0.035	-0.080	0.060	100	No
Mean thickness of parsorbitalis L	-0.027	0.037	-0.100	0.042	100	No
Mean thickness of parsorbitalis R	0.000	0.037	-0.071	0.071	100	No
Mean thickness of parstriangularis L	0.067	0.035	-0.001	0.132	100	No
Mean thickness of parstriangularis R	-0.013	0.034	-0.078	0.053	100	No
Mean thickness of pericalcarine L	0.018	0.034	-0.050	0.084	100	No
Mean thickness of pericalcarine R	-0.074	0.034	-0.141	-0.010	100	Yes*
Mean thickness of postcentral L	0.020	0.031	-0.042	0.082	100	No
Mean thickness of postcentral R	0.050	0.031	-0.011	0.109	100	No
Mean thickness of posteriorcingulate L	0.033	0.036	-0.036	0.103	100	No
Mean thickness of posteriorcingulate R	0.040	0.035	-0.027	0.108	100	No
Mean thickness of precentral L	0.041	0.028	-0.014	0.095	100	No
Mean thickness of precentral R	0.048	0.029	-0.009	0.101	100	No
Mean thickness of precuneus L	0.005	0.031	-0.054	0.067	100	No
Mean thickness of precuneus R	0.034	0.032	-0.024	0.100	100	No
Mean thickness of rostralanteriorcingulate L	-0.039	0.040	-0.122	0.037	100	No
Mean thickness of rostralanteriorcingulate R	0.001	0.037	-0.072	0.075	100	No
Mean thickness of rostralmiddlefrontal L	0.015	0.031	-0.043	0.077	100	No
Mean thickness of rostralmiddlefrontal R	0.001	0.033	-0.060	0.062	100	No
Mean thickness of superiorfrontal L	-0.004	0.028	-0.053	0.055	100	No
Mean thickness of superiorfrontal R	-0.009	0.028	-0.062	0.047	100	No
Mean thickness of superiorparietal L	0.022	0.030	-0.033	0.084	100	No
Mean thickness of superiorparietal R	-0.016	0.029	-0.073	0.040	100	No
Mean thickness of superiortemporal L	-0.021	0.030	-0.081	0.036	100	No
Mean thickness of superiortemporal R	-0.014	0.032	-0.076	0.047	100	No
Mean thickness of supramarginal L	-0.070	0.033	-0.131	-0.004	100	Yes*
Mean thickness of supramarginal R	-0.023	0.033	-0.090	0.036	100	No
Mean thickness of transversetemporal L	0.007	0.036	-0.067	0.077	100	No
Mean thickness of transversetemporal R	0.027	0.034	-0.042	0.089	100	No
Volume of caudalanteriorcingulate L	0.003	0.031	-0.059	0.062	100	No
Volume of caudalanteriorcingulate R	-0.004	0.030	-0.061	0.058	100	No
Volume of caudalmiddlefrontal L	0.010	0.030	-0.050	0.068	100	No
Volume of caudalmiddlefrontal R	0.017	0.029	-0.036	0.075	100	No

Volume of cuneus L	-0.009	0.028	-0.065	0.048	100	No
Volume of cuneus R	0.012	0.028	-0.044	0.066	100	No
Volume of entorhinal L	0.017	0.031	-0.043	0.075	100	No
Volume of entorhinal R	0.051	0.036	-0.016	0.118	100	No
Volume of fusiform L	-0.008	0.031	-0.070	0.052	100	No
Volume of fusiform R	0.008	0.031	-0.053	0.067	100	No
Volume of inferiorparietal L	-0.043	0.030	-0.099	0.015	100	No
Volume of inferiorparietal R	-0.005	0.031	-0.065	0.054	100	No
Volume of inferiortemporal L	-0.106	0.030	-0.164	-0.048	100	Yes*
Volume of inferiortemporal R	-0.026	0.032	-0.086	0.038	100	No
Volume of insula L	0.013	0.028	-0.042	0.067	100	No
Volume of insula R	0.024	0.030	-0.037	0.081	100	No
Volume of isthmuscingulate L	0.007	0.031	-0.053	0.064	100	No
Volume of isthmuscingulate R	-0.022	0.031	-0.086	0.038	100	No
Volume of lateraloccipital L	0.003	0.028	-0.053	0.057	100	No
Volume of lateraloccipital R	0.003	0.029	-0.055	0.060	100	No
Volume of lateralorbitofrontal L	-0.007	0.031	-0.066	0.052	100	No
Volume of lateralorbitofrontal R	0.030	0.031	-0.031	0.090	100	No
Volume of lingual L	-0.023	0.028	-0.078	0.031	100	No
Volume of lingual R	0.011	0.029	-0.047	0.067	100	No
Volume of medialorbitofrontal L	-0.039	0.031	-0.101	0.028	100	No
Volume of medialorbitofrontal R	0.021	0.032	-0.044	0.078	100	No
Volume of middletemporal L	0.004	0.029	-0.049	0.063	100	No
Volume of middletemporal R	-0.041	0.030	-0.101	0.021	100	No
Volume of paracentral L	0.016	0.032	-0.047	0.081	100	No
Volume of paracentral R	-0.035	0.030	-0.093	0.026	100	No
Volume of parahippocampal L	-0.002	0.031	-0.060	0.061	100	No
Volume of parahippocampal R	0.002	0.033	-0.060	0.069	100	No
Volume of parsopercularis L	-0.031	0.030	-0.088	0.027	100	No
Volume of parsopercularis R	-0.015	0.029	-0.072	0.038	100	No
Volume of parsorbitalis L	-0.029	0.032	-0.093	0.032	100	No
Volume of parsorbitalis R	0.008	0.031	-0.052	0.069	100	No
Volume of parstriangularis L	0.023	0.030	-0.032	0.078	100	No
Volume of parstriangularis R	-0.011	0.031	-0.069	0.046	100	No
Volume of pericalcarine L	-0.023	0.027	-0.077	0.029	100	No
Volume of pericalcarine R	-0.014	0.026	-0.068	0.039	100	No
Volume of postcentral L	-0.001	0.029	-0.058	0.056	100	No
Volume of postcentral R	0.010	0.030	-0.047	0.071	100	No
Volume of posteriorcingulate L	0.001	0.032	-0.060	0.063	100	No
Volume of posteriorcingulate R	0.013	0.032	-0.049	0.079	100	No
Volume of precentral L	0.010	0.029	-0.046	0.065	100	No
Volume of precentral R	0.038	0.029	-0.017	0.092	100	No
Volume of precuneus L	-0.001	0.031	-0.058	0.058	100	No
Volume of precuneus R	0.007	0.028	-0.045	0.063	100	No

Volume of rostralanteriorcingulate L	-0.022	0.032	-0.088	0.039	100	No
Volume of rostralanteriorcingulate R	-0.008	0.033	-0.071	0.055	100	No
Volume of rostralmiddlefrontal L	-0.026	0.030	-0.083	0.032	100	No
Volume of rostralmiddlefrontal R	0.001	0.029	-0.054	0.060	100	No
Volume of superiorfrontal L	-0.008	0.029	-0.066	0.049	100	No
Volume of superiorfrontal R	-0.049	0.028	-0.103	0.004	100	No
Volume of superiorparietal L	0.043	0.028	-0.015	0.096	100	No
Volume of superiorparietal R	0.015	0.029	-0.042	0.071	100	No
Volume of superiortemporal L	0.021	0.030	-0.038	0.078	100	No
Volume of superiortemporal R	-0.018	0.029	-0.072	0.038	100	No
Volume of supramarginal L	-0.053	0.029	-0.107	0.004	100	No
Volume of supramarginal R	-0.039	0.030	-0.096	0.019	100	No
Volume of transversetemporal L	0.028	0.033	-0.036	0.091	100	No
Volume of transversetemporal R	0.009	0.032	-0.053	0.071	100	No
Volume of accumbens L	-0.001	0.039	-0.077	0.075	100	No
Volume of accumbens R	0.063	0.037	-0.006	0.133	100	No
Volume of amygdala L	-0.046	0.041	-0.124	0.035	100	No
Volume of amygdala R	0.031	0.040	-0.049	0.109	100	No
Volume of caudate L	-0.017	0.032	-0.081	0.045	100	No
Volume of caudate R	0.010	0.031	-0.050	0.069	100	No
Volume of hippocampus L	0.003	0.038	-0.070	0.073	100	No
Volume of hippocampus R	-0.052	0.036	-0.122	0.023	100	No
Volume of pallidum L	-0.031	0.036	-0.102	0.041	100	No
Volume of pallidum R	-0.011	0.037	-0.088	0.062	100	No
Volume of putamen L	0.014	0.036	-0.052	0.084	100	No
Volume of putamen R	0.048	0.036	-0.023	0.121	100	No
Volume of thalamus L	-0.026	0.030	-0.086	0.035	100	No
Volume of thalamus R	-0.038	0.031	-0.098	0.020	100	No
Mean FA in anterior corona radiata L	-0.042	0.028	-0.097	0.012	100	No
Mean FA in anterior corona radiata R	0.003	0.028	-0.051	0.057	100	No
Mean FA in anterior limb of internal capsule L	0.001	0.029	-0.055	0.056	100	No
Mean FA in anterior limb of internal capsule R	-0.015	0.029	-0.074	0.039	100	No
Mean FA in body of corpus callosum	-0.015	0.026	-0.068	0.036	100	No
Mean FA in cerebral peduncle L	0.011	0.028	-0.044	0.064	100	No
Mean FA in cerebral peduncle R	-0.037	0.028	-0.094	0.017	100	No
Mean FA in cingulum cingulate gyrus L	0.055	0.028	0.003	0.112	100	Yes*
Mean FA in cingulum cingulate gyrus R	0.039	0.026	-0.009	0.090	100	No
Mean FA in cingulum hippocampus L	0.019	0.029	-0.037	0.078	100	No
Mean FA in cingulum hippocampus R	0.004	0.029	-0.052	0.060	100	No
Mean FA in corticospinal tract L	0.003	0.034	-0.064	0.066	100	No
Mean FA in corticospinal tract R	-0.017	0.034	-0.082	0.050	100	No
Mean FA in external capsule L	0.038	0.027	-0.016	0.092	100	No
Mean FA in external capsule R	-0.001	0.028	-0.054	0.055	100	No
Mean FA in fornix cres+stria terminalis L	0.001	0.027	-0.052	0.054	100	No

Mean FA in fornix cres+stria terminalis R	-0.023	0.032	-0.085	0.037	100	No
Mean FA in fornix	-0.018	0.026	-0.067	0.032	100	No
Mean FA in genu of corpus callosum	-0.017	0.028	-0.076	0.039	100	No
Mean FA in inferior cerebellar peduncle L	-0.010	0.025	-0.062	0.039	100	No
Mean FA in inferior cerebellar peduncle R	0.030	0.028	-0.021	0.085	100	No
Mean FA in medial lemniscus L	-0.001	0.030	-0.060	0.058	100	No
Mean FA in medial lemniscus R	0.013	0.029	-0.045	0.072	100	No
Mean FA in middle cerebellar peduncle	0.024	0.032	-0.043	0.087	100	No
Mean FA in pontine crossing tract	0.046	0.036	-0.026	0.118	100	No
Mean FA in posterior corona radiata L	0.016	0.031	-0.044	0.075	100	No
Mean FA in posterior corona radiata R	0.010	0.028	-0.045	0.065	100	No
Mean FA in posterior limb of internal capsule L	0.007	0.025	-0.042	0.053	100	No
Mean FA in posterior limb of internal capsule R	0.045	0.024	-0.002	0.091	100	No
Mean FA in posterior thalamic radiation L	-0.015	0.030	-0.071	0.043	100	No
Mean FA in posterior thalamic radiation R	-0.068	0.029	-0.124	-0.011	100	Yes*
Mean FA in retrolenticular part of internal capsule L	-0.027	0.029	-0.083	0.028	100	No
Mean FA in retrolenticular part of internal capsule R	0.008	0.029	-0.048	0.065	100	No
Mean FA in sagittal stratum L	-0.021	0.028	-0.074	0.035	100	No
Mean FA in sagittal stratum R	-0.045	0.029	-0.100	0.010	100	No
Mean FA in splenium of corpus callosum	0.049	0.027	-0.001	0.098	100	No
Mean FA in superior cerebellar peduncle L	0.003	0.029	-0.053	0.060	100	No
Mean FA in superior cerebellar peduncle R	0.000	0.028	-0.054	0.055	100	No
Mean FA in superior corona radiata L	-0.053	0.027	-0.105	0.001	100	No
Mean FA in superior corona radiata R	0.011	0.030	-0.045	0.071	100	No
Mean FA in superior fronto-occipital fasciculus L	-0.025	0.033	-0.088	0.041	100	No
Mean FA in superior fronto-occipital fasciculus R	-0.026	0.031	-0.086	0.038	100	No
Mean FA in superior longitudinal fasciculus L	0.023	0.028	-0.031	0.079	100	No
Mean FA in superior longitudinal fasciculus R	0.022	0.029	-0.033	0.079	100	No
Mean FA in tapetum L	-0.075	0.032	-0.139	-0.013	100	Yes*
Mean FA in tapetum R	-0.030	0.032	-0.090	0.034	100	No
Mean FA in uncinate fasciculus L	0.025	0.029	-0.031	0.080	100	No
Mean FA in uncinate fasciculus R	-0.048	0.029	-0.104	0.006	100	No
Mean L1 in anterior corona radiata L	-0.005	0.029	-0.061	0.054	100	No
Mean L1 in anterior corona radiata R	0.011	0.029	-0.045	0.071	100	No
Mean L1 in anterior limb of internal capsule L	0.000	0.032	-0.061	0.059	100	No
Mean L1 in anterior limb of internal capsule R	-0.019	0.032	-0.079	0.040	100	No
Mean L1 in body of corpus callosum	0.070	0.034	0.002	0.136	100	Yes*
Mean L1 in cerebral peduncle L	-0.047	0.034	-0.114	0.021	100	No
Mean L1 in cerebral peduncle R	0.003	0.034	-0.072	0.067	100	No
Mean L1 in cingulum cingulate gyrus L	0.039	0.032	-0.019	0.098	100	No
Mean L1 in cingulum cingulate gyrus R	0.000	0.032	-0.060	0.062	100	No
Mean L1 in cingulum hippocampus L	-0.008	0.033	-0.075	0.056	100	No
Mean L1 in cingulum hippocampus R	-0.039	0.034	-0.102	0.027	100	No
Mean L1 in corticospinal tract L	0.001	0.032	-0.061	0.065	100	No

Mean L1 in corticospinal tract R	-0.030	0.032	-0.097	0.033	100	No
Mean L1 in external capsule L	0.049	0.030	-0.012	0.106	100	No
Mean L1 in external capsule R	0.076	0.031	0.011	0.136	100	Yes*
Mean L1 in fornix cres+stria terminalis L	0.002	0.035	-0.063	0.067	100	No
Mean L1 in fornix cres+stria terminalis R	0.032	0.036	-0.039	0.102	100	No
Mean L1 in fornix	0.027	0.028	-0.029	0.084	100	No
Mean L1 in genu of corpus callosum	-0.053	0.036	-0.121	0.019	100	No
Mean L1 in inferior cerebellar peduncle L	0.008	0.035	-0.066	0.076	100	No
Mean L1 in inferior cerebellar peduncle R	-0.012	0.035	-0.084	0.053	100	No
Mean L1 in medial lemniscus L	-0.030	0.029	-0.083	0.028	100	No
Mean L1 in medial lemniscus R	-0.016	0.031	-0.077	0.046	100	No
Mean L1 in middle cerebellar peduncle	0.015	0.031	-0.044	0.075	100	No
Mean L1 in pontine crossing tract	-0.015	0.027	-0.067	0.038	100	No
Mean L1 in posterior corona radiata L	-0.046	0.028	-0.100	0.009	100	No
Mean L1 in posterior corona radiata R	0.012	0.029	-0.048	0.066	100	No
Mean L1 in posterior limb of internal capsule L	-0.014	0.031	-0.073	0.047	100	No
Mean L1 in posterior limb of internal capsule R	-0.050	0.030	-0.107	0.011	100	No
Mean L1 in posterior thalamic radiation L	-0.003	0.032	-0.065	0.062	100	No
Mean L1 in posterior thalamic radiation R	-0.036	0.032	-0.103	0.024	100	No
Mean L1 in retrolenticular part of internal capsule L	-0.034	0.034	-0.101	0.027	100	No
Mean L1 in retrolenticular part of internal capsule R	-0.037	0.034	-0.103	0.030	100	No
Mean L1 in sagittal stratum L	-0.010	0.033	-0.072	0.055	100	No
Mean L1 in sagittal stratum R	-0.037	0.031	-0.101	0.023	100	No
Mean L1 in splenium of corpus callosum	0.009	0.032	-0.054	0.075	100	No
Mean L1 in superior cerebellar peduncle L	0.010	0.031	-0.050	0.070	100	No
Mean L1 in superior cerebellar peduncle R	0.018	0.030	-0.041	0.078	100	No
Mean L1 in superior corona radiata L	0.009	0.026	-0.045	0.062	100	No
Mean L1 in superior corona radiata R	0.028	0.027	-0.025	0.078	100	No
Mean L1 in superior fronto-occipital fasciculus L	0.008	0.031	-0.051	0.069	100	No
Mean L1 in superior fronto-occipital fasciculus R	-0.037	0.033	-0.104	0.029	100	No
Mean L1 in superior longitudinal fasciculus L	0.015	0.031	-0.048	0.076	100	No
Mean L1 in superior longitudinal fasciculus R	-0.015	0.030	-0.071	0.044	100	No
Mean L1 in tapetum L	-0.029	0.034	-0.090	0.033	100	No
Mean L1 in tapetum R	-0.069	0.035	-0.137	-0.005	100	Yes*
Mean L1 in uncinate fasciculus L	0.019	0.035	-0.050	0.086	100	No
Mean L1 in uncinate fasciculus R	-0.033	0.034	-0.104	0.031	100	No
Mean RD in anterior corona radiata L	0.042	0.024	-0.003	0.090	100	No
Mean RD in anterior corona radiata R	0.006	0.024	-0.038	0.054	100	No
Mean RD in anterior limb of internal capsule L	0.018	0.028	-0.037	0.073	100	No
Mean RD in anterior limb of internal capsule R	0.006	0.028	-0.048	0.061	100	No
Mean RD in body of corpus callosum	0.054	0.028	0.000	0.110	100	Yes*
Mean RD in cerebral peduncle L	-0.030	0.028	-0.083	0.026	100	No
Mean RD in cerebral peduncle R	0.041	0.029	-0.016	0.101	100	No
Mean RD in cingulum cingulate gyrus L	-0.055	0.029	-0.114	0.000	100	Yes*

Mean RD in cingulum cingulate gyrus R	-0.063	0.029	-0.117	-0.006	100	Yes*
Mean RD in cingulum hippocampus L	-0.026	0.031	-0.091	0.034	100	No
Mean RD in cingulum hippocampus R	-0.019	0.030	-0.079	0.039	100	No
Mean RD in corticospinal tract L	0.014	0.026	-0.036	0.065	100	No
Mean RD in corticospinal tract R	0.011	0.027	-0.041	0.063	100	No
Mean RD in external capsule L	0.009	0.025	-0.040	0.055	100	No
Mean RD in external capsule R	0.062	0.027	0.008	0.109	100	Yes*
Mean RD in fornix cres+stria terminalis L	-0.004	0.027	-0.054	0.049	100	No
Mean RD in fornix cres+stria terminalis R	0.030	0.030	-0.031	0.086	100	No
Mean RD in fornix	0.025	0.024	-0.022	0.073	100	No
Mean RD in genu of corpus callosum	0.007	0.028	-0.047	0.064	100	No
Mean RD in inferior cerebellar peduncle L	0.036	0.031	-0.025	0.096	100	No
Mean RD in inferior cerebellar peduncle R	-0.023	0.030	-0.078	0.035	100	No
Mean RD in medial lemniscus L	-0.020	0.024	-0.065	0.029	100	No
Mean RD in medial lemniscus R	-0.024	0.025	-0.073	0.023	100	No
Mean RD in middle cerebellar peduncle	-0.019	0.029	-0.076	0.040	100	No
Mean RD in pontine crossing tract	-0.047	0.022	-0.093	-0.003	100	Yes*
Mean RD in posterior corona radiata L	-0.046	0.023	-0.093	-0.001	100	Yes*
Mean RD in posterior corona radiata R	-0.005	0.023	-0.052	0.040	100	No
Mean RD in posterior limb of internal capsule L	-0.016	0.029	-0.069	0.039	100	No
Mean RD in posterior limb of internal capsule R	-0.079	0.028	-0.134	-0.022	100	Yes*
Mean RD in posterior thalamic radiation L	0.001	0.024	-0.046	0.045	100	No
Mean RD in posterior thalamic radiation R	0.039	0.025	-0.012	0.087	100	No
Mean RD in retrolenticular part of internal capsule L	0.013	0.029	-0.047	0.069	100	No
Mean RD in retrolenticular part of internal capsule R	-0.012	0.030	-0.068	0.044	100	No
Mean RD in sagittal stratum L	0.018	0.029	-0.037	0.075	100	No
Mean RD in sagittal stratum R	0.021	0.026	-0.032	0.071	100	No
Mean RD in splenium of corpus callosum	-0.051	0.028	-0.102	0.005	100	No
Mean RD in superior cerebellar peduncle L	0.015	0.027	-0.039	0.069	100	No
Mean RD in superior cerebellar peduncle R	0.020	0.029	-0.038	0.076	100	No
Mean RD in superior corona radiata L	0.055	0.026	0.006	0.108	100	Yes*
Mean RD in superior corona radiata R	0.027	0.026	-0.024	0.075	100	No
Mean RD in superior fronto-occipital fasciculus L	0.045	0.026	-0.006	0.092	100	No
Mean RD in superior fronto-occipital fasciculus R	0.003	0.027	-0.051	0.051	100	No
Mean RD in superior longitudinal fasciculus L	-0.022	0.027	-0.075	0.029	100	No
Mean RD in superior longitudinal fasciculus R	-0.028	0.027	-0.084	0.024	100	No
Mean RD in tapetum L	0.028	0.027	-0.025	0.078	100	No
Mean RD in tapetum R	-0.015	0.026	-0.069	0.033	100	No
Mean RD in uncinate fasciculus L	0.004	0.030	-0.053	0.063	100	No
Mean RD in uncinate fasciculus R	0.041	0.031	-0.020	0.097	100	No
Spos_1	-0.023	0.038	-0.100	0.053	100	No
Spos_2	-0.041	0.037	-0.111	0.034	100	No
Spos_3	-0.016	0.037	-0.084	0.057	100	No
Spos_4	0.017	0.039	-0.057	0.095	100	No

Spos_5	-0.025	0.040	-0.103	0.052	100	No
Spos_6	0.007	0.039	-0.069	0.078	100	No
Spos_7	-0.005	0.038	-0.078	0.071	100	No
Spos_8	-0.047	0.037	-0.121	0.023	100	No
Spos_9	-0.005	0.043	-0.090	0.079	100	No
Spos_10	-0.040	0.041	-0.126	0.041	100	No
Spos_11	-0.018	0.042	-0.102	0.059	100	No
Spos_12	0.033	0.040	-0.046	0.114	100	No
Spos_13	0.014	0.039	-0.061	0.092	100	No
Spos_14	0.030	0.039	-0.044	0.111	100	No
Spos_15	-0.013	0.040	-0.093	0.067	100	No
Spos_16	0.033	0.036	-0.036	0.104	100	No
Spos_17	-0.013	0.040	-0.090	0.066	100	No
Spos_18	-0.004	0.040	-0.082	0.071	100	No
Spos_19	-0.010	0.044	-0.095	0.080	100	No
Spos_20	0.043	0.039	-0.032	0.113	100	No
Spos_21	-0.015	0.040	-0.091	0.059	100	No
Spos_22	-0.012	0.040	-0.092	0.062	100	No
Spos_23	-0.054	0.041	-0.133	0.027	100	No
Spos_24	0.027	0.040	-0.055	0.104	100	No
Spos_25	-0.004	0.041	-0.088	0.074	100	No
Spos_26	0.012	0.043	-0.070	0.100	100	No
Spos_27	-0.077	0.038	-0.149	0.000	100	No
Spos_28	-0.013	0.040	-0.093	0.064	100	No
Spos_29	0.048	0.038	-0.027	0.123	100	No
Spos_30	0.026	0.039	-0.051	0.105	100	No
Spos_31	0.014	0.041	-0.065	0.101	100	No
Spos_32	0.054	0.038	-0.022	0.129	100	No
Spos_33	-0.029	0.041	-0.110	0.047	100	No
Spos_34	0.007	0.041	-0.076	0.085	100	No
Spos_35	-0.013	0.037	-0.086	0.057	100	No
Spos_36	0.006	0.041	-0.073	0.087	100	No
Spos_37	-0.011	0.040	-0.089	0.064	100	No
Spos_38	-0.002	0.039	-0.075	0.078	100	No
Spos_39	-0.016	0.040	-0.096	0.064	100	No
Spos_40	-0.013	0.041	-0.092	0.063	100	No
Spos_41	0.012	0.039	-0.066	0.085	100	No
Spos_42	-0.001	0.040	-0.081	0.073	100	No
Spos_43	-0.012	0.040	-0.086	0.069	100	No
Spos_44	-0.006	0.039	-0.085	0.070	100	No
Spos_45	0.020	0.038	-0.052	0.093	100	No
Spos_46	-0.010	0.039	-0.082	0.062	100	No
Spos_47	-0.015	0.038	-0.090	0.060	100	No
Spos_48	0.045	0.039	-0.029	0.123	100	No

Spos_49	-0.002	0.039	-0.080	0.072	100	No
Spos_50	0.039	0.039	-0.042	0.115	100	No
Spos_51	0.021	0.041	-0.055	0.105	100	No
Spos_52	-0.078	0.041	-0.159	0.001	100	No
Spos_53	0.038	0.041	-0.043	0.119	100	No
Spos_54	-0.003	0.040	-0.079	0.077	100	No
Spos_55	0.043	0.041	-0.037	0.124	100	No
Sneg_1	-0.096	0.037	-0.169	-0.025	100	Yes*
Sneg_2	0.020	0.041	-0.062	0.100	100	No
Sneg_3	-0.066	0.039	-0.138	0.012	100	No
Sneg_4	0.021	0.037	-0.054	0.093	100	No
Sneg_5	-0.092	0.040	-0.168	-0.013	100	Yes*
Sneg_6	0.018	0.039	-0.058	0.092	100	No
Sneg_7	0.004	0.039	-0.073	0.083	100	No
Sneg_8	-0.036	0.038	-0.115	0.043	100	No
Sneg_9	-0.009	0.040	-0.088	0.070	100	No
Sneg_10	-0.043	0.040	-0.120	0.039	100	No
Sneg_11	-0.004	0.042	-0.089	0.073	100	No
Sneg_12	-0.020	0.041	-0.103	0.059	100	No
Sneg_13	0.012	0.040	-0.070	0.088	100	No
Sneg_14	0.040	0.037	-0.031	0.116	100	No
Sneg_15	-0.037	0.039	-0.116	0.041	100	No
Sneg_16	0.015	0.035	-0.055	0.084	100	No
Sneg_17	-0.043	0.039	-0.120	0.034	100	No
Sneg_18	0.019	0.040	-0.058	0.097	100	No
Sneg_19	-0.071	0.041	-0.151	0.010	100	No
Sneg_20	-0.038	0.039	-0.112	0.039	100	No
Sneg_21	0.040	0.040	-0.036	0.118	100	No
Sneg_22	-0.020	0.041	-0.100	0.059	100	No
Sneg_23	-0.011	0.038	-0.083	0.068	100	No
Sneg_24	-0.021	0.041	-0.101	0.058	100	No
Sneg_25	-0.015	0.040	-0.087	0.062	100	No
Sneg_26	0.032	0.039	-0.045	0.107	100	No
Sneg_27	-0.038	0.040	-0.115	0.038	100	No
Sneg_28	-0.025	0.040	-0.108	0.050	100	No
Sneg_29	0.076	0.038	-0.003	0.153	100	No
Sneg_30	-0.037	0.041	-0.117	0.045	100	No
Sneg_31	-0.013	0.039	-0.088	0.063	100	No
Sneg_32	-0.090	0.037	-0.162	-0.017	100	Yes*
Sneg_33	-0.032	0.041	-0.114	0.049	100	No
Sneg_34	0.003	0.041	-0.080	0.082	100	No
Sneg_35	-0.029	0.041	-0.106	0.052	100	No
Sneg_36	-0.001	0.040	-0.081	0.073	100	No
Sneg_37	-0.036	0.041	-0.115	0.044	100	No

Sneg_38	-0.038	0.041	-0.122	0.044	100	No
Sneg_39	0.024	0.038	-0.051	0.098	100	No
Sneg_40	-0.044	0.042	-0.125	0.041	100	No
Sneg_41	-0.027	0.037	-0.099	0.043	100	No
Sneg_42	-0.018	0.039	-0.097	0.057	100	No
Sneg_43	0.029	0.043	-0.054	0.107	100	No
Sneg_44	-0.093	0.039	-0.167	-0.020	100	Yes*
Sneg_45	-0.018	0.041	-0.101	0.062	100	No
Sneg_46	-0.051	0.038	-0.128	0.024	100	No
Sneg_47	0.053	0.042	-0.033	0.132	100	No
Sneg_48	-0.047	0.040	-0.127	0.027	100	No
Sneg_49	-0.004	0.039	-0.079	0.075	100	No
Sneg_50	-0.007	0.040	-0.086	0.073	100	No
Sneg_51	-0.040	0.042	-0.120	0.044	100	No
Sneg_52	0.038	0.042	-0.047	0.118	100	No
Sneg_53	0.018	0.041	-0.063	0.097	100	No
Sneg_54	0.031	0.043	-0.057	0.116	100	No
Sneg_55	0.023	0.041	-0.058	0.101	100	No
Median z-statistic (amygdala)for faces-shapes contrast	-0.038	0.031	-0.100	0.025	100	No
Median z-statistic for faces activation	-0.020	0.025	-0.070	0.025	100	No
Median z-statistic for shapes activation	-0.010	0.026	-0.059	0.042	100	No
Median z-statistic for faces-shapes contrast	0.021	0.032	-0.041	0.085	100	No
90th percentile of z-statistic (amygdala)for faces-shapes contrast	-0.081	0.032	-0.142	-0.015	100	Yes*
90th percentile of z-statistic for faces activation	-0.018	0.023	-0.061	0.026	100	No
90th percentile of z-statistic for shapes activation	-0.020	0.026	-0.069	0.032	100	No
90th percentile of z-statistic for faces-shapes contrast	0.045	0.029	-0.012	0.099	100	No
ALCDEP Walters2018	-0.065	0.040	-0.144	0.011	100	No
AN Watson2019	-0.055	0.042	-0.137	0.023	100	No
ASD Grove2019	0.055	0.041	-0.032	0.131	100	No
BD PGC4 2025	0.035	0.041	-0.041	0.120	100	No
BMI Locke2015	0.000	0.041	-0.082	0.073	100	No
Bngf Konieczny2025	-0.024	0.039	-0.100	0.053	100	No
CAD Nikpay2015	0.066	0.040	-0.010	0.146	100	No
CCL11 Konieczny2025	-0.002	0.042	-0.088	0.076	100	No
CCL2 Konieczny2025	0.014	0.040	-0.063	0.091	100	No
CCL3 Konieczny2025	0.023	0.044	-0.060	0.108	100	No
CCL4 Konieczny2025	-0.029	0.043	-0.112	0.056	100	No
CCL7 MCP3 Konieczny2025	-0.011	0.041	-0.090	0.073	100	No
CRP Said2022	0.019	0.043	-0.063	0.106	100	No
CSF1 Konieczny2025	0.057	0.039	-0.019	0.137	100	No
CSF3 Konieczny2025	0.015	0.043	-0.066	0.102	100	No
CTACK Konieczny2025	-0.035	0.039	-0.106	0.044	100	No
CUD Johnson2020	-0.025	0.043	-0.112	0.059	100	No
CXCL1 Konieczny2025	-0.039	0.042	-0.116	0.046	100	No

CXCL10 Konieczny2025	-0.056	0.040	-0.130	0.023	100	No
CXCL12 Konieczny2025	0.034	0.041	-0.044	0.114	100	No
CXCL9 Konieczny2025	-0.022	0.040	-0.096	0.059	100	No
FGFb Konieczny2025	0.015	0.042	-0.071	0.098	100	No
GAD FinnGen2024	0.057	0.042	-0.026	0.138	100	No
HbA1c Willems2023	-0.024	0.041	-0.104	0.055	100	No
HDL Graham2021	-0.094	0.043	-0.175	-0.009	100	Yes*
HGF Konieczny2025	0.052	0.042	-0.033	0.130	100	No
IFNg Konieczny2025	0.009	0.034	-0.056	0.073	100	No
IL10 Konieczny2025	-0.031	0.037	-0.103	0.040	100	No
IL13 Konieczny2025	0.015	0.030	-0.041	0.076	100	No
IL16 Konieczny2025	0.081	0.043	0.001	0.165	100	Yes*
IL17 Konieczny2025	0.009	0.037	-0.063	0.082	100	No
IL18 Konieczny2025	0.072	0.042	-0.012	0.154	100	No
IL1b Konieczny2025	0.011	0.040	-0.066	0.096	100	No
IL1RA Konieczny2025	-0.021	0.041	-0.097	0.061	100	No
IL2 Konieczny2025	0.044	0.041	-0.040	0.125	100	No
IL2RA Konieczny2025	-0.004	0.041	-0.086	0.072	100	No
IL4 Konieczny2025	0.056	0.032	-0.006	0.117	100	No
IL5 Konieczny2025	0.017	0.036	-0.054	0.087	100	No
IL6 Konieczny2025	0.009	0.041	-0.074	0.088	100	No
IL7 Konieczny2025	-0.001	0.032	-0.061	0.064	100	No
IL8 Konieczny2025	0.004	0.040	-0.072	0.084	100	No
IL9 Konieczny2025	-0.013	0.040	-0.088	0.065	100	No
LDL Graham2021	0.053	0.041	-0.028	0.131	100	No
MDD PGC4_2025	-0.009	0.039	-0.085	0.067	100	No
MIF Konieczny2025	0.060	0.043	-0.026	0.140	100	No
NEUROT DeMoor2015	0.019	0.043	-0.062	0.103	100	No
OCD PGC3 2018	0.030	0.043	-0.054	0.116	100	No
PDGFBB Konieczny2025	-0.009	0.041	-0.089	0.068	100	No
PTSD Nievergelt2024	-0.043	0.040	-0.120	0.034	100	No
RANTES Konieczny2025	-0.018	0.039	-0.093	0.060	100	No
SCF Konieczny2025	0.037	0.040	-0.040	0.117	100	No
SCGFb Konieczny2025	0.017	0.040	-0.064	0.094	100	No
SCZ Trubetskoy2022	0.045	0.042	-0.037	0.125	100	No
T2D Verma2024	0.107	0.041	0.034	0.190	100	Yes*
TNFa Konieczny2025	0.059	0.032	0.000	0.122	100	No
TNFb Konieczny2025	-0.010	0.031	-0.070	0.051	100	No
TRAIL Konieczny2025	-0.042	0.040	-0.121	0.029	100	No
TRIG Graham2021	0.112	0.038	0.037	0.187	100	Yes*
VEGF Konieczny2025	0.012	0.041	-0.064	0.096	100	No

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CI, confidence interval; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder;

*FA, fractional anisotropy; FGFb, basic fibroblast growth factor; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; SD, standard deviation; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor; VIP, variable inclusion probability. *Statistical significance at 95%CI*

Table A15. Summary of consensus clustering models with dimensionally-reduced input features among the MDD sample of OSR.

Model	Clusters	Class counts	Sil	DB	q-value
GM	2	CI0: 5, CI 1: 172	0.786	0.353	N.S.
DTI	3	CI0: 36, CI1: 121, CI2: 1	0.014	3.372	N.S.
rs-fMRI	2	CI0: 3, CI1: 110	0.062	2.301	N.S.
t-fMRI	5	CI0: 27, CI1: 14, CI2: 32, CI3: 8, CI4: 1	0.283	0.940	N.S.
PGSs	5	CI0: 24, CI1: 31, CI2: 20, CI3: 24, CI4: 71	0.023	3.939	N.S.
Stress	4	CI0: 10, CI1: 1, CI2: 74, CI3: 40	0.509	0.564	N.S.

Abbreviations: *CI*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *N.S.*, not significant; *PGSs*, polygenic scores; *rs-fMRI*, resting-state *fMRI*; *Sil*, Silhouette score; *t-fMRI*, task-based *fMRI*.

Table A16. Summary of consensus clustering models with dimensionally-reduced input features among the MDD and BD sample of OSR.

Model	Clusters	Class counts	Sil	DB	q-value
GM	4	CI0: 59, CI1: 273, CI2: CI45, CI3: 46	0.022	5.183	N.S.
DTI	5	CI0: 63, CI1: 99, CI2: 57, CI3: 31, CI4: 94	0.032	4.075	N.S.
rs-fMRI	4	CI0: 7, CI1: 60, CI2: 18, CI3: 131	0.009	5.195	N.S.
t-fMRI	4	CI0: 10, CI1: 86, CI2: 40, CI3: 38	0.260	1.108	N.S.
PGSs	4	CI0: 89, CI1: 75, CI2: 91, CI3: 144	0.015	5.222	N.S.
Stress	3	CI0: 14, CI1: 80, CI2: 171	0.478	0.772	N.S.

Abbreviations: *CI*, cluster; *DB*, Davies-Bouldin index; *DTI*, diffusion tensor imaging; *fMRI*, functional magnetic resonance imaging; *GM*, grey matter; *N.S.*, not significant; *PGSs*, polygenic scores; *rs-fMRI*, resting-state *fMRI*; *Sil*, Silhouette score; *t-fMRI*, task-based *fMRI*.

Table A17. Input feature comparisons between clusters resulting from the significant stratification models among the MDD sample of the OSR dataset.

Model	Variable	C10	C11	Statistic	Effect size	p-value	q-value
DTI	Mean FA in anterior corona radiata L	0.44 ± 0.02	0.41 ± 0.02	9.34	1.480	<0.001	<0.001*
DTI	Mean FA in anterior corona radiata R	0.45 ± 0.02	0.41 ± 0.02	9.00	1.426	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule L	0.58 ± 0.02	0.55 ± 0.02	8.89	1.408	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule R	0.58 ± 0.03	0.56 ± 0.02	6.71	1.062	<0.001	<0.001*
DTI	Mean FA in body of corpus callosum	0.69 ± 0.02	0.66 ± 0.02	10.91	1.729	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle L	0.71 ± 0.02	0.68 ± 0.02	9.64	1.526	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle R	0.71 ± 0.02	0.67 ± 0.02	9.53	1.509	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus L	0.59 ± 0.03	0.56 ± 0.03	4548.00	0.870	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus R	0.54 ± 0.03	0.52 ± 0.03	4.67	0.740	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus L	0.49 ± 0.03	0.46 ± 0.03	5.08	0.804	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus R	0.48 ± 0.03	0.46 ± 0.03	3.57	0.565	<0.001	<0.001*
DTI	Mean FA in corticospinal tract L	0.56 ± 0.03	0.53 ± 0.04	5.63	0.892	<0.001	<0.001*
DTI	Mean FA in corticospinal tract R	0.54 ± 0.03	0.51 ± 0.03	4.81	0.762	<0.001	<0.001*
DTI	Mean FA in external capsule L	0.44 ± 0.02	0.41 ± 0.02	8.70	1.379	<0.001	<0.001*
DTI	Mean FA in external capsule R	0.42 ± 0.02	0.40 ± 0.02	6.78	1.073	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis L	0.56 ± 0.03	0.52 ± 0.03	5104.00	1.325	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis R	0.55 ± 0.03	0.52 ± 0.03	4678.00	1.031	<0.001	<0.001*
DTI	Mean FA in fornix	0.46 ± 0.07	0.43 ± 0.06	3897.00	0.433	0.007	0.009*
DTI	Mean FA in genu of corpus callosum	0.69 ± 0.03	0.66 ± 0.02	8.24	1.305	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle L	0.56 ± 0.02	0.54 ± 0.03	5.83	0.924	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle R	0.56 ± 0.02	0.53 ± 0.03	5.78	0.916	<0.001	<0.001*
DTI	Mean FA in medial lemniscus L	0.59 ± 0.02	0.56 ± 0.03	4561.00	0.930	<0.001	<0.001*
DTI	Mean FA in medial lemniscus R	0.59 ± 0.02	0.57 ± 0.03	4539.00	0.886	<0.001	<0.001*
DTI	Mean FA in middle cerebellar peduncle	0.56 ± 0.02	0.54 ± 0.02	4703.00	0.977	<0.001	<0.001*
DTI	Mean FA in pontine crossing tract	0.48 ± 0.04	0.45 ± 0.03	4522.00	0.825	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata L	0.47 ± 0.02	0.44 ± 0.02	5298.00	1.404	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata R	0.48 ± 0.02	0.45 ± 0.02	5030.00	1.156	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule L	0.69 ± 0.03	0.66 ± 0.03	5144.00	1.272	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule R	0.68 ± 0.02	0.64 ± 0.03	8.19	1.297	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation L	0.60 ± 0.03	0.57 ± 0.03	6.94	1.100	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation R	0.59 ± 0.03	0.57 ± 0.03	6.02	0.953	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule L	0.61 ± 0.02	0.58 ± 0.03	4940.00	1.141	<0.001	<0.001*

DTI	Mean FA in retrolenticular part of internal capsule R	0.57 ± 0.02	0.55 ± 0.03	4.94	0.782	<0.001	<0.001*
DTI	Mean FA in sagittal stratum L	0.57 ± 0.03	0.53 ± 0.03	8.43	1.336	<0.001	<0.001*
DTI	Mean FA in sagittal stratum R	0.56 ± 0.02	0.54 ± 0.02	6.93	1.098	<0.001	<0.001*
DTI	Mean FA in splenium of corpus callosum	0.78 ± 0.02	0.75 ± 0.02	9.88	1.566	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle L	0.69 ± 0.03	0.66 ± 0.03	7.91	1.253	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle R	0.69 ± 0.03	0.65 ± 0.03	7.69	1.218	<0.001	<0.001*
DTI	Mean FA in superior corona radiata L	0.48 ± 0.02	0.45 ± 0.02	8.40	1.330	<0.001	<0.001*
DTI	Mean FA in superior corona radiata R	0.47 ± 0.02	0.44 ± 0.02	8.09	1.282	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus L	0.46 ± 0.04	0.43 ± 0.03	4578.00	0.906	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus R	0.45 ± 0.04	0.43 ± 0.03	3.65	0.578	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus L	0.51 ± 0.02	0.48 ± 0.03	8.68	1.375	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus R	0.49 ± 0.02	0.47 ± 0.02	6.32	1.002	<0.001	<0.001*
DTI	Mean FA in tapetum L	0.60 ± 0.05	0.56 ± 0.05	4.98	0.788	<0.001	<0.001*
DTI	Mean FA in tapetum R	0.58 ± 0.05	0.52 ± 0.05	7.42	1.175	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus L	0.50 ± 0.03	0.47 ± 0.04	5.33	0.844	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus R	0.51 ± 0.04	0.49 ± 0.04	4.83	0.765	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	-4.79	-0.759	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata R	0.12 ± 0.00	0.12 ± 0.01	-3.87	-0.612	<0.001	<0.001*
DTI	Mean AD in anterior limb of internal capsule L	0.12 ± 0.00	0.12 ± 0.00	-2.89	-0.459	0.004	0.006*
DTI	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	-1.82	-0.289	0.070	0.085
DTI	Mean AD in body of corpus callosum	0.16 ± 0.00	0.16 ± 0.01	-3.70	-0.586	<0.001	<0.001*
DTI	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	0.21	0.033	0.836	0.853
DTI	Mean AD in cerebral peduncle R	0.14 ± 0.01	0.14 ± 0.01	0.62	0.098	0.536	0.572
DTI	Mean AD in cingulum cingulate gyrus L	0.13 ± 0.01	0.13 ± 0.01	-0.94	-0.149	0.349	0.380
DTI	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	-1.92	-0.303	0.057	0.070
DTI	Mean AD in cingulum hippocampus L	0.13 ± 0.01	0.12 ± 0.01	1.33	0.211	0.184	0.212
DTI	Mean AD in cingulum hippocampus R	0.13 ± 0.01	0.13 ± 0.01	0.44	0.069	0.664	0.688
DTI	Mean AD in corticospinal tract L	0.12 ± 0.01	0.12 ± 0.01	1.60	0.253	0.112	0.132
DTI	Mean AD in corticospinal tract R	0.12 ± 0.01	0.12 ± 0.01	2.17	0.344	0.031	0.039*
DTI	Mean AD in external capsule L	0.11 ± 0.00	0.11 ± 0.00	2786.50	-0.157	0.249	0.282
DTI	Mean AD in external capsule R	0.11 ± 0.00	0.11 ± 0.00	-1.13	-0.179	0.260	0.292
DTI	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.13 ± 0.01	3363.50	0.081	0.395	0.428
DTI	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	3069.00	-0.053	0.865	0.877
DTI	Mean AD in fornix	0.23 ± 0.03	0.22 ± 0.02	3313.50	0.115	0.499	0.536
DTI	Mean AD in genu of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	1769.00	-0.713	<0.001	<0.001*
DTI	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.01	0.12 ± 0.00	3876.00	0.465	0.008	0.011*

DTI	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.01	0.12 ± 0.00	4.22	0.668	<0.001	<0.001*
DTI	Mean AD in medial lemniscus L	0.13 ± 0.01	0.12 ± 0.01	3.40	0.538	<0.001	0.001*
DTI	Mean AD in medial lemniscus R	0.13 ± 0.01	0.13 ± 0.01	3.15	0.499	0.002	0.003*
DTI	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	3747.50	0.433	0.029	0.036*
DTI	Mean AD in pontine crossing tract	0.11 ± 0.01	0.11 ± 0.01	4.06	0.642	<0.001	<0.001*
DTI	Mean AD in posterior corona radiata L	0.12 ± 0.01	0.12 ± 0.00	2594.50	-0.291	0.069	0.084
DTI	Mean AD in posterior corona radiata R	0.12 ± 0.01	0.13 ± 0.01	-3.68	-0.583	<0.001	<0.001*
DTI	Mean AD in posterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	3274.00	0.081	0.590	0.615
DTI	Mean AD in posterior limb of internal capsule R	0.13 ± 0.01	0.13 ± 0.01	0.16	0.025	0.875	0.882
DTI	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	-0.36	-0.056	0.723	0.744
DTI	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.01	2948.50	-0.076	0.555	0.584
DTI	Mean AD in retrolenticular part of internal capsule L	0.13 ± 0.01	0.13 ± 0.01	-0.60	-0.095	0.551	0.584
DTI	Mean AD in retrolenticular part of internal capsule R	0.13 ± 0.00	0.14 ± 0.01	-3.63	-0.574	<0.001	<0.001*
DTI	Mean AD in sagittal stratum L	0.14 ± 0.01	0.14 ± 0.01	-1.07	-0.170	0.286	0.319
DTI	Mean AD in sagittal stratum R	0.14 ± 0.01	0.14 ± 0.01	2029.00	-0.568	<0.001	<0.001*
DTI	Mean AD in splenium of corpus callosum	0.16 ± 0.00	0.16 ± 0.00	-3.05	-0.483	0.003	0.004*
DTI	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	1.61	0.255	0.110	0.130
DTI	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	1.54	0.244	0.125	0.147
DTI	Mean AD in superior corona radiata L	0.11 ± 0.00	0.11 ± 0.00	2379.00	-0.412	0.010	0.014*
DTI	Mean AD in superior corona radiata R	0.11 ± 0.00	0.11 ± 0.00	-3.56	-0.563	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.01	0.11 ± 0.01	2732.50	-0.279	0.180	0.209
DTI	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.11 ± 0.01	2832.00	-0.224	0.320	0.351
DTI	Mean AD in superior longitudinal fasciculus L	0.11 ± 0.00	0.12 ± 0.00	-2.54	-0.402	0.012	0.016*
DTI	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	-4.65	-0.736	<0.001	<0.001*
DTI	Mean AD in tapetum L	0.16 ± 0.01	0.16 ± 0.01	-1.00	-0.159	0.317	0.351
DTI	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	3121.00	-0.028	0.994	0.994
DTI	Mean AD in uncinate fasciculus L	0.13 ± 0.01	0.13 ± 0.01	2.11	0.334	0.036	0.045*
DTI	Mean AD in uncinate fasciculus R	0.13 ± 0.01	0.13 ± 0.01	2.25	0.356	0.026	0.033*
DTI	Mean RD in anterior corona radiata L	0.06 ± 0.00	0.06 ± 0.00	-10.72	-1.698	<0.001	<0.001*
DTI	Mean RD in anterior corona radiata R	0.06 ± 0.00	0.06 ± 0.00	-10.36	-1.641	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.05 ± 0.00	-10.56	-1.673	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule R	0.04 ± 0.00	0.05 ± 0.00	-7.42	-1.175	<0.001	<0.001*
DTI	Mean RD in body of corpus callosum	0.04 ± 0.00	0.05 ± 0.00	-11.01	-1.744	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle L	0.04 ± 0.00	0.04 ± 0.00	-9.67	-1.532	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle R	0.04 ± 0.00	0.04 ± 0.00	-9.12	-1.444	<0.001	<0.001*

DTI	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.05 ± 0.00	-7.53	-1.193	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.05 ± 0.00	-7.45	-1.180	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.06 ± 0.00	-3.38	-0.535	<0.001	0.001*
DTI	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.06 ± 0.00	-3.30	-0.522	0.001	0.002*
DTI	Mean RD in corticospinal tract L	0.05 ± 0.00	0.05 ± 0.00	2080.50	-0.558	<0.001	<0.001*
DTI	Mean RD in corticospinal tract R	0.05 ± 0.00	0.05 ± 0.00	2392.50	-0.401	0.012	0.015*
DTI	Mean RD in external capsule L	0.06 ± 0.00	0.06 ± 0.00	1138.50	-1.216	<0.001	<0.001*
DTI	Mean RD in external capsule R	0.06 ± 0.00	0.06 ± 0.00	-5.60	-0.887	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis L	0.05 ± 0.00	0.06 ± 0.01	1371.50	-1.008	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis R	0.05 ± 0.00	0.06 ± 0.01	1442.00	-0.977	<0.001	<0.001*
DTI	Mean RD in fornix	0.11 ± 0.03	0.12 ± 0.03	2755.50	-0.152	0.207	0.237
DTI	Mean RD in genu of corpus callosum	0.04 ± 0.00	0.05 ± 0.00	-9.96	-1.578	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	-4.01	-0.636	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	2208.50	-0.526	0.002	0.002*
DTI	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	2453.00	-0.363	0.021	0.027*
DTI	Mean RD in medial lemniscus R	0.05 ± 0.00	0.05 ± 0.00	-2.36	-0.373	0.020	0.026*
DTI	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	-3.60	-0.571	<0.001	<0.001*
DTI	Mean RD in pontine crossing tract	0.05 ± 0.00	0.05 ± 0.00	-1.66	-0.263	0.099	0.119
DTI	Mean RD in posterior corona radiata L	0.06 ± 0.00	0.06 ± 0.00	1283.50	-1.104	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata R	0.06 ± 0.00	0.06 ± 0.00	-8.18	-1.295	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule L	0.03 ± 0.00	0.04 ± 0.00	1058.00	-1.328	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	-8.68	-1.374	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.01	-5.55	-0.880	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	-5.54	-0.877	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.00	0.05 ± 0.00	1314.50	-1.141	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	-7.79	-1.233	<0.001	<0.001*
DTI	Mean RD in sagittal stratum L	0.05 ± 0.00	0.06 ± 0.00	-8.54	-1.352	<0.001	<0.001*
DTI	Mean RD in sagittal stratum R	0.05 ± 0.00	0.06 ± 0.00	-8.33	-1.320	<0.001	<0.001*
DTI	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.04 ± 0.00	-11.66	-1.847	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle L	0.04 ± 0.01	0.05 ± 0.00	-5.20	-0.823	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle R	0.04 ± 0.01	0.05 ± 0.00	-5.41	-0.857	<0.001	<0.001*
DTI	Mean RD in superior corona radiata L	0.05 ± 0.00	0.05 ± 0.00	777.00	-1.546	<0.001	<0.001*
DTI	Mean RD in superior corona radiata R	0.05 ± 0.00	0.06 ± 0.00	-11.52	-1.824	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.00	0.06 ± 0.00	1248.00	-1.078	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.00	0.06 ± 0.00	1531.50	-0.860	<0.001	<0.001*

DTI	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	-9.38	-1.485	<0.001	<0.001*
DTI	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.00	0.06 ± 0.00	-9.33	-1.477	<0.001	<0.001*
DTI	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	2107.00	-0.597	<0.001	<0.001*
DTI	Mean RD in tapetum R	0.06 ± 0.01	0.07 ± 0.01	1630.50	-0.820	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus L	0.05 ± 0.00	0.06 ± 0.00	2084.50	-0.575	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus R	0.05 ± 0.00	0.06 ± 0.00	-2.92	-0.463	0.004	0.006*
t-fMRI	Median z-statistic (amygdala) for faces-shapes contrast	0.26 ± 0.73	1.01 ± 0.63	-4.64	-1.131	<0.001	<0.001*
t-fMRI	Median z-statistic for faces activation	0.87 ± 0.63	2.61 ± 0.59	-11.73	-2.856	<0.001	<0.001*
t-fMRI	Median z-statistic for shapes activation	0.87 ± 0.63	2.28 ± 0.63	-9.15	-2.229	<0.001	<0.001*
t-fMRI	Median z-statistic for faces-shapes contrast	0.88 ± 0.85	3.61 ± 1.22	29.00	-2.390	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic (amygdala) for faces-shapes	1.61 ± 0.91	2.68 ± 0.83	271.00	-1.231	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces activation	3.56 ± 1.32	6.95 ± 1.09	-11.90	-2.897	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for shapes activation	3.16 ± 1.04	5.53 ± 0.96	-9.75	-2.375	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces-shapes contrast	3.12 ± 1.66	7.28 ± 1.64	-10.29	-2.507	<0.001	<0.001*
t-fMRI	Left amygdala habituation for faces condition	0.05 ± 0.37	-0.02 ± 0.25	0.85	0.208	0.396	0.432
t-fMRI	Right amygdala habituation for faces condition	-0.05 ± 0.37	0.05 ± 0.23	510.00	-0.375	0.083	0.111
t-fMRI	Left amygdala habituation for shapes condition	0.08 ± 0.46	0.00 ± 0.21	763.00	0.261	0.386	0.432
t-fMRI	Right amygdala habituation for shapes condition	0.02 ± 0.40	-0.00 ± 0.19	620.00	0.082	0.549	0.549
PGSs	ADHD Demontis2022	-0.04 ± 0.93	0.05 ± 1.02	-0.61	-0.092	0.546	0.668
PGSs	ALCDEP Walters2018	0.01 ± 1.00	0.01 ± 1.05	0.02	0.002	0.987	0.987
PGSs	AN Watson2019	-0.11 ± 0.99	0.09 ± 1.00	-1.32	-0.201	0.190	0.367
PGSs	ASD Grove2019	-0.02 ± 1.02	0.10 ± 0.93	-0.80	-0.122	0.427	0.565
PGSs	BD PGC4 2025	-0.07 ± 1.04	-0.10 ± 1.01	0.23	0.035	0.817	0.876
PGSs	BMI Locke2015	-0.13 ± 0.91	0.10 ± 1.03	-1.53	-0.233	0.128	0.256
PGSs	bNGF Konieczny2025	-0.36 ± 1.01	0.34 ± 0.91	-4.74	-0.725	<0.001	<0.001*
PGSs	CAD Nikpay2015	0.15 ± 0.97	-0.25 ± 0.95	2.68	0.410	0.008	0.023*
PGSs	CCL11 Konieczny2025	-0.13 ± 0.96	0.27 ± 0.99	2760.00	-0.413	0.008	0.023*
PGSs	CCL2 Konieczny2025	-0.14 ± 0.85	0.05 ± 0.87	3026.00	-0.221	0.069	0.153
PGSs	CCL3 Konieczny2025	0.07 ± 0.95	-0.08 ± 1.03	0.96	0.146	0.339	0.484
PGSs	CCL4 Konieczny2025	0.18 ± 0.94	-0.07 ± 1.04	3974.00	0.244	0.258	0.418
PGSs	CCL7 Konieczny2025	-0.12 ± 0.99	0.08 ± 1.04	-1.24	-0.189	0.217	0.383
PGSs	CRP Said2022	-0.22 ± 1.06	0.18 ± 0.95	-2.60	-0.397	0.010	0.026*
PGSs	CSF1 Konieczny2025	0.05 ± 1.03	-0.15 ± 0.98	1.26	0.192	0.210	0.383
PGSs	CSF3 Konieczny2025	-0.09 ± 0.76	-0.05 ± 1.12	3596.50	-0.047	0.966	0.983
PGSs	CTACK Konieczny2025	-0.48 ± 0.85	0.50 ± 0.90	1488.00	-1.122	<0.001	<0.001*
PGSs	CUD Johnson2020	-0.06 ± 0.98	0.06 ± 0.92	-0.87	-0.133	0.384	0.536
PGSs	CXCL1 Konieczny2025	0.04 ± 0.95	0.10 ± 0.94	-0.39	-0.059	0.699	0.791
PGSs	CXCL10 Konieczny2025	-0.36 ± 1.08	0.38 ± 0.84	2125.00	-0.758	<0.001	<0.001*
PGSs	CXCL12 Konieczny2025	-0.08 ± 1.05	0.10 ± 0.95	3238.50	-0.172	0.247	0.418
PGSs	CXCL9 Konieczny2025	-0.44 ± 0.89	0.34 ± 0.83	-5.93	-0.906	<0.001	<0.001*

PGSs	FGFb Konieczny2025	0.10 ± 0.83	-0.06 ± 1.02	1.15	0.176	0.252	0.418
PGSs	GAD FinnGen2024	0.03 ± 0.96	0.09 ± 1.03	-0.39	-0.060	0.696	0.791
PGSs	HbA1c Willems2023	0.03 ± 0.95	-0.02 ± 1.03	0.29	0.045	0.769	0.854
PGSs	HDL Graham2021	-0.09 ± 0.95	-0.00 ± 1.08	-0.57	-0.088	0.567	0.681
PGSs	HGF Konieczny2025	-0.19 ± 1.07	0.26 ± 1.09	2781.00	-0.413	0.010	0.026*
PGSs	IFNg Konieczny2025	-0.52 ± 0.75	0.62 ± 0.89	-8.95	-1.368	<0.001	<0.001*
PGSs	IL10 Konieczny2025	-0.54 ± 0.82	0.52 ± 0.88	-8.10	-1.238	<0.001	<0.001*
PGSs	IL13 Konieczny2025	-0.59 ± 0.71	0.70 ± 0.78	-11.22	-1.714	<0.001	<0.001*
PGSs	IL16 Konieczny2025	0.02 ± 1.02	-0.06 ± 1.11	3846.50	0.082	0.463	0.579
PGSs	IL17 Konieczny2025	-0.61 ± 0.79	0.58 ± 0.78	-9.83	-1.501	<0.001	<0.001*
PGSs	IL18 Konieczny2025	0.19 ± 0.99	-0.03 ± 1.03	4025.50	0.217	0.196	0.368
PGSs	IL1b Konieczny2025	-0.01 ± 0.96	-0.16 ± 0.89	0.99	0.152	0.323	0.472
PGSs	IL1RA Konieczny2025	-0.27 ± 1.01	0.08 ± 0.97	-2.34	-0.358	0.020	0.049*
PGSs	IL2 Konieczny2025	-0.30 ± 0.93	0.26 ± 0.92	-3.93	-0.601	<0.001	<0.001*
PGSs	IL2RA Konieczny2025	-0.06 ± 0.96	0.10 ± 1.00	3363.50	-0.159	0.442	0.565
PGSs	IL4 Konieczny2025	-0.62 ± 0.73	0.66 ± 0.76	-11.22	-1.713	<0.001	<0.001*
PGSs	IL5 Konieczny2025	-0.66 ± 0.72	0.67 ± 0.73	-12.01	-1.835	<0.001	<0.001*
PGSs	IL6 Konieczny2025	-0.28 ± 0.97	0.24 ± 0.94	-3.53	-0.539	<0.001	0.002*
PGSs	IL7 Konieczny2025	-0.61 ± 0.69	0.62 ± 0.72	-11.32	-1.729	<0.001	<0.001*
PGSs	IL8 Konieczny2025	-0.54 ± 0.89	0.51 ± 0.85	-7.94	-1.212	<0.001	<0.001*
PGSs	IL9 Konieczny2025	-0.40 ± 0.81	0.45 ± 0.93	-6.35	-0.970	<0.001	<0.001*
PGSs	LDL Graham2021	0.08 ± 0.96	-0.05 ± 0.94	0.86	0.131	0.393	0.536
PGSs	MDD PGC4 2025	0.00 ± 0.98	0.04 ± 0.94	-0.23	-0.035	0.818	0.876
PGSs	MIF Konieczny2025	-0.22 ± 0.99	0.13 ± 0.98	-2.30	-0.352	0.022	0.052
PGSs	NEUROT DeMoor2015	0.03 ± 0.95	-0.03 ± 0.96	0.46	0.070	0.648	0.762
PGSs	OCD PGC3 2018	0.01 ± 1.07	0.17 ± 0.96	-1.05	-0.160	0.295	0.454
PGSs	PDGFBB Konieczny2025	-0.23 ± 1.04	0.21 ± 0.97	2681.50	-0.432	0.004	0.012*
PGSs	PTSD Nievergelt2024	-0.06 ± 0.93	0.10 ± 0.97	-1.10	-0.167	0.275	0.434
PGSs	RANTES Konieczny2025	0.01 ± 1.00	0.30 ± 0.89	3038.50	-0.313	0.075	0.155
PGSs	SCF Konieczny2025	-0.02 ± 1.16	-0.03 ± 1.02	0.07	0.011	0.943	0.976
PGSs	SCGFb Konieczny2025	-0.25 ± 1.08	0.21 ± 0.91	-3.00	-0.458	0.003	0.010*
PGSs	SCZ Trubetskoy2022	-0.12 ± 0.98	-0.10 ± 0.95	-0.12	-0.019	0.902	0.949
PGSs	T2D Verma2024	-0.05 ± 0.92	0.21 ± 1.02	-1.79	-0.274	0.075	0.155
PGSs	TNFa Konieczny2025	-0.58 ± 0.78	0.71 ± 0.73	773.00	-1.689	<0.001	<0.001*
PGSs	TNFb Konieczny2025	-0.67 ± 0.74	0.73 ± 0.63	-13.34	-2.037	<0.001	<0.001*
PGSs	TRAIL Konieczny2025	-0.15 ± 0.95	0.04 ± 1.21	3284.50	-0.165	0.310	0.465
PGSs	TRIG Graham2021	-0.03 ± 0.97	0.05 ± 1.08	3361.00	-0.071	0.438	0.565
PGSs	VEGF Konieczny2025	-0.22 ± 1.02	0.16 ± 1.01	-2.41	-0.369	0.017	0.042*
Multimodal	Area of caudalanteriorcingulate L	1341.75 ± 278.97	1046.49 ± 189.21	2.94	1.500	0.005	0.073
Multimodal	Area of caudalanteriorcingulate R	906.75 ± 259.46	764.61 ± 172.44	156.00	0.791	0.360	0.716
Multimodal	Area of caudalmiddlefrontal L	2798.25 ± 774.14	2345.87 ± 398.83	180.00	1.053	0.116	0.367
Multimodal	Area of caudalmiddlefrontal R	2815.75 ± 837.86	2158.46 ± 418.35	183.00	1.452	0.099	0.322
Multimodal	Area of cuneus L	1424.00 ± 234.75	1919.25 ± 412.30	-2.37	-1.206	0.021	0.102

Multimodal	Area of cuneus R	1454.00 ± 337.26	1788.13 ± 415.69	-1.57	-0.801	0.121	0.378
Multimodal	Area of entorhinal L	781.50 ± 125.50	408.25 ± 122.49	236.00	3.007	0.002	0.073
Multimodal	Area of entorhinal R	791.50 ± 117.84	396.70 ± 186.52	235.00	2.122	0.002	0.073
Multimodal	Area of fusiform L	2839.00 ± 593.05	2617.44 ± 332.56	1.23	0.627	0.224	0.551
Multimodal	Area of fusiform R	2743.75 ± 679.11	2500.30 ± 437.94	1.04	0.532	0.301	0.644
Multimodal	Area of inferiorparietal L	3959.75 ± 591.47	4227.51 ± 707.29	-0.74	-0.377	0.463	0.806
Multimodal	Area of inferiorparietal R	4838.25 ± 962.39	4940.67 ± 739.87	104.00	-0.135	0.633	0.876
Multimodal	Area of inferiortemporal L	3513.00 ± 680.63	3312.44 ± 484.54	0.78	0.400	0.436	0.781
Multimodal	Area of inferiortemporal R	3574.00 ± 271.28	3382.31 ± 525.40	0.72	0.367	0.474	0.813
Multimodal	Area of insula L	1886.50 ± 101.11	1750.20 ± 262.16	183.00	0.524	0.099	0.322
Multimodal	Area of insula R	1807.75 ± 176.64	1876.39 ± 288.35	115.00	-0.239	0.859	0.948
Multimodal	Area of isthmuscingulate L	650.25 ± 347.59	956.70 ± 213.35	57.00	-1.366	0.078	0.271
Multimodal	Area of isthmuscingulate R	409.25 ± 335.88	858.48 ± 231.00	20.50	-1.872	0.006	0.073
Multimodal	Area of lateraloccipital L	4493.25 ± 1127.43	4736.85 ± 685.92	104.00	-0.337	0.633	0.876
Multimodal	Area of lateraloccipital R	4245.00 ± 965.92	4734.49 ± 682.14	-1.36	-0.693	0.179	0.496
Multimodal	Area of lateralorbitofrontal L	3322.50 ± 528.83	2920.26 ± 348.55	2.17	1.106	0.034	0.147
Multimodal	Area of lateralorbitofrontal R	3202.50 ± 437.75	2922.10 ± 403.40	1.34	0.684	0.185	0.500
Multimodal	Area of lingual L	2376.75 ± 271.43	2816.89 ± 531.87	46.50	-0.832	0.041	0.167
Multimodal	Area of lingual R	1991.75 ± 155.80	2840.69 ± 612.79	27.00	-1.400	0.010	0.078
Multimodal	Area of medialorbitofrontal L	1781.25 ± 134.58	1606.46 ± 171.15	2.00	1.018	0.050	0.197
Multimodal	Area of medialorbitofrontal R	1516.00 ± 290.10	1523.97 ± 178.98	101.00	-0.042	0.576	0.860
Multimodal	Area of middletemporal L	3841.25 ± 765.73	4005.70 ± 691.95	-0.46	-0.234	0.649	0.881
Multimodal	Area of middletemporal R	3774.50 ± 785.13	3939.56 ± 608.63	-0.52	-0.264	0.607	0.870
Multimodal	Area of paracentral L	1945.00 ± 448.75	1548.82 ± 203.35	200.00	1.769	0.034	0.147
Multimodal	Area of paracentral R	2032.25 ± 372.81	1536.51 ± 230.46	224.00	2.048	0.006	0.073
Multimodal	Area of parahippocampal L	840.25 ± 517.93	659.02 ± 117.98	127.00	1.110	0.902	0.964
Multimodal	Area of parahippocampal R	802.75 ± 319.19	663.10 ± 125.91	168.50	0.977	0.209	0.534
Multimodal	Area of parsopercularis L	1440.25 ± 335.61	1352.05 ± 211.15	134.00	0.398	0.754	0.919
Multimodal	Area of parsopercularis R	1557.75 ± 253.14	1418.02 ± 244.58	1.11	0.564	0.273	0.614
Multimodal	Area of parsorbitalis L	796.75 ± 146.37	679.54 ± 88.08	183.00	1.263	0.099	0.322
Multimodal	Area of parsorbitalis R	678.50 ± 96.47	681.84 ± 105.43	119.50	-0.031	0.956	0.984
Multimodal	Area of parstriangularis L	1646.75 ± 440.26	1498.03 ± 242.71	151.00	0.575	0.437	0.781
Multimodal	Area of parstriangularis R	1547.75 ± 63.32	1409.75 ± 277.31	0.99	0.503	0.328	0.678
Multimodal	Area of pericalcarine L	1048.25 ± 92.77	1272.02 ± 300.83	-1.47	-0.751	0.146	0.426
Multimodal	Area of pericalcarine R	1016.50 ± 243.93	1376.28 ± 354.03	-1.99	-1.017	0.050	0.197

Multimodal	Area of postcentral L	4972.00 ± 500.22	4390.77 ± 463.18	202.00	1.235	0.030	0.131
Multimodal	Area of postcentral R	4329.00 ± 652.02	4112.26 ± 498.92	0.83	0.422	0.411	0.764
Multimodal	Area of posteriorcingulate L	1248.75 ± 157.19	1196.49 ± 245.86	143.50	0.213	0.566	0.860
Multimodal	Area of posteriorcingulate R	1120.50 ± 258.21	1171.87 ± 222.93	-0.44	-0.226	0.659	0.885
Multimodal	Area of precentral L	5008.25 ± 732.69	4504.64 ± 532.64	179.00	0.915	0.123	0.381
Multimodal	Area of precentral R	4546.00 ± 790.84	4293.05 ± 570.86	0.84	0.429	0.404	0.760
Multimodal	Area of precuneus L	3937.00 ± 661.07	3475.87 ± 458.31	1.90	0.970	0.062	0.231
Multimodal	Area of precuneus R	3670.50 ± 387.40	3619.33 ± 515.34	0.19	0.099	0.846	0.947
Multimodal	Area of rostralanteriorcingulate L	1563.25 ± 438.67	1097.00 ± 210.18	208.00	2.035	0.020	0.096
Multimodal	Area of rostralanteriorcingulate R	957.50 ± 201.55	789.51 ± 172.32	1.87	0.955	0.066	0.240
Multimodal	Area of rostralmiddlefrontal L	5390.25 ± 840.60	3870.10 ± 651.39	227.00	2.270	0.004	0.073
Multimodal	Area of rostralmiddlefrontal R	5268.00 ± 1041.34	3953.77 ± 651.30	3.77	1.924	<0.001	0.073
Multimodal	Area of superiorfrontal L	9184.25 ± 1414.99	7812.72 ± 939.25	204.00	1.401	0.026	0.117
Multimodal	Area of superiorfrontal R	10884.25 ± 1973.62	8875.79 ± 1114.48	211.00	1.696	0.016	0.090
Multimodal	Area of superiorparietal L	4268.25 ± 794.21	4164.98 ± 509.94	0.38	0.194	0.705	0.908
Multimodal	Area of superiorparietal R	4613.00 ± 634.23	4174.77 ± 629.71	1.35	0.687	0.183	0.500
Multimodal	Area of superiortemporal L	4987.00 ± 414.99	4760.66 ± 749.76	0.59	0.303	0.554	0.859
Multimodal	Area of superiortemporal R	4260.50 ± 1045.75	4486.25 ± 620.23	-0.68	-0.345	0.501	0.836
Multimodal	Area of supramarginal L	3786.50 ± 1041.18	3486.38 ± 685.98	126.50	0.419	0.913	0.968
Multimodal	Area of supramarginal R	3874.75 ± 1219.28	3245.30 ± 647.62	166.00	0.907	0.235	0.566
Multimodal	Area of transversetemporal L	370.75 ± 142.83	391.59 ± 91.55	123.00	-0.218	0.989	0.993
Multimodal	Area of transversetemporal R	191.75 ± 95.73	290.07 ± 70.14	54.50	-1.357	0.067	0.243
Multimodal	Mean thickness of caudalanteriorcingulate L	1.36 ± 0.06	2.17 ± 0.42	30.50	-1.952	0.013	0.084
Multimodal	Mean thickness of caudalanteriorcingulate R	1.39 ± 0.13	2.05 ± 0.39	30.00	-1.716	0.012	0.083
Multimodal	Mean thickness of caudalmiddlefrontal L	1.66 ± 0.13	2.26 ± 0.31	22.00	-1.924	0.007	0.073
Multimodal	Mean thickness of caudalmiddlefrontal R	1.70 ± 0.12	2.23 ± 0.30	26.00	-1.795	0.009	0.078
Multimodal	Mean thickness of cuneus L	1.32 ± 0.11	1.74 ± 0.29	35.00	-1.459	0.018	0.096
Multimodal	Mean thickness of cuneus R	1.33 ± 0.10	1.77 ± 0.27	32.00	-1.660	0.015	0.088
Multimodal	Mean thickness of entorhinal L	1.89 ± 0.26	2.86 ± 0.49	17.00	-1.977	0.004	0.073
Multimodal	Mean thickness of entorhinal R	1.76 ± 0.15	2.93 ± 0.54	12.00	-2.212	0.003	0.073
Multimodal	Mean thickness of fusiform L	1.56 ± 0.19	2.32 ± 0.41	28.00	-1.882	0.011	0.082
Multimodal	Mean thickness of fusiform R	1.64 ± 0.10	2.34 ± 0.39	33.00	-1.792	0.016	0.090
Multimodal	Mean thickness of inferiorparietal L	1.55 ± 0.10	2.16 ± 0.29	22.50	-2.076	0.007	0.073
Multimodal	Mean thickness of inferiorparietal R	1.44 ± 0.07	2.12 ± 0.33	18.00	-2.115	0.005	0.073
Multimodal	Mean thickness of inferiortemporal L	1.81 ± 0.09	2.50 ± 0.29	11.00	-2.390	0.003	0.073
Multimodal	Mean thickness of inferiortemporal R	1.80 ± 0.24	2.45 ± 0.30	17.00	-2.185	0.004	0.073

Multimodal	Mean thickness of insula L	1.41 ± 0.12	2.62 ± 0.57	20.00	-2.147	0.006	0.073
Multimodal	Mean thickness of insula R	1.40 ± 0.11	2.58 ± 0.56	23.00	-2.119	0.007	0.073
Multimodal	Mean thickness of isthmuscingulate L	1.49 ± 0.28	2.03 ± 0.24	13.00	-2.258	0.003	0.073
Multimodal	Mean thickness of isthmuscingulate R	1.49 ± 0.27	2.03 ± 0.27	18.00	-1.966	0.005	0.073
Multimodal	Mean thickness of lateraloccipital L	1.67 ± 0.07	2.00 ± 0.20	23.00	-1.681	0.007	0.073
Multimodal	Mean thickness of lateraloccipital R	1.69 ± 0.04	2.03 ± 0.22	31.00	-1.553	0.013	0.084
Multimodal	Mean thickness of lateralorbitofrontal L	1.62 ± 0.07	2.30 ± 0.31	13.00	-2.237	0.003	0.073
Multimodal	Mean thickness of lateralorbitofrontal R	1.59 ± 0.07	2.23 ± 0.30	15.00	-2.197	0.004	0.073
Multimodal	Mean thickness of lingual L	1.38 ± 0.08	1.89 ± 0.26	22.50	-1.963	0.007	0.073
Multimodal	Mean thickness of lingual R	1.41 ± 0.11	1.92 ± 0.26	20.00	-1.963	0.006	0.073
Multimodal	Mean thickness of medialorbitofrontal L	1.69 ± 0.09	2.16 ± 0.28	31.00	-1.731	0.013	0.084
Multimodal	Mean thickness of medialorbitofrontal R	1.62 ± 0.14	2.24 ± 0.30	19.00	-2.047	0.005	0.073
Multimodal	Mean thickness of middletemporal L	1.72 ± 0.08	2.39 ± 0.30	14.50	-2.224	0.003	0.073
Multimodal	Mean thickness of middletemporal R	1.79 ± 0.22	2.39 ± 0.31	19.00	-1.901	0.005	0.073
Multimodal	Mean thickness of paracentral L	1.63 ± 0.10	2.18 ± 0.37	35.00	-1.514	0.018	0.096
Multimodal	Mean thickness of paracentral R	1.60 ± 0.10	2.13 ± 0.38	37.00	-1.416	0.021	0.102
Multimodal	Mean thickness of parahippocampal L	2.00 ± 0.29	2.40 ± 0.33	39.00	-1.206	0.024	0.113
Multimodal	Mean thickness of parahippocampal R	1.86 ± 0.25	2.28 ± 0.39	40.00	-1.093	0.026	0.117
Multimodal	Mean thickness of parsopercularis L	1.51 ± 0.16	2.19 ± 0.35	23.00	-1.965	0.007	0.073
Multimodal	Mean thickness of parsopercularis R	1.42 ± 0.13	2.17 ± 0.35	17.00	-2.172	0.004	0.073
Multimodal	Mean thickness of parsorbitalis L	1.60 ± 0.06	2.27 ± 0.36	25.00	-1.887	0.008	0.076
Multimodal	Mean thickness of parsorbitalis R	1.67 ± 0.12	2.29 ± 0.33	21.00	-1.881	0.006	0.073
Multimodal	Mean thickness of parstriangularis L	1.60 ± 0.13	2.10 ± 0.21	12.00	-2.357	0.003	0.073
Multimodal	Mean thickness of parstriangularis R	1.70 ± 0.05	2.10 ± 0.22	24.00	-1.844	0.008	0.074
Multimodal	Mean thickness of pericalcarine L	1.27 ± 0.11	1.55 ± 0.19	29.00	-1.476	0.012	0.082
Multimodal	Mean thickness of pericalcarine R	1.44 ± 0.10	1.57 ± 0.20	53.00	-0.646	0.061	0.231
Multimodal	Mean thickness of postcentral L	1.69 ± 0.13	1.91 ± 0.18	36.00	-1.219	0.020	0.096
Multimodal	Mean thickness of postcentral R	1.70 ± 0.09	1.89 ± 0.20	47.00	-0.981	0.042	0.170
Multimodal	Mean thickness of posteriorscingulate L	1.31 ± 0.14	2.02 ± 0.35	21.00	-2.060	0.006	0.073
Multimodal	Mean thickness of posteriorscingulate R	1.19 ± 0.06	2.03 ± 0.36	14.50	-2.366	0.003	0.073
Multimodal	Mean thickness of precentral L	1.64 ± 0.08	2.28 ± 0.38	36.00	-1.713	0.020	0.096
Multimodal	Mean thickness of precentral R	1.57 ± 0.14	2.27 ± 0.37	23.50	-1.888	0.007	0.074
Multimodal	Mean thickness of precuneus L	1.36 ± 0.07	2.07 ± 0.39	36.00	-1.851	0.020	0.096
Multimodal	Mean thickness of precuneus R	1.36 ± 0.06	2.06 ± 0.38	34.00	-1.851	0.017	0.094
Multimodal	Mean thickness of rostralanteriorcingulate L	1.50 ± 0.08	2.24 ± 0.43	34.00	-1.746	0.017	0.094
Multimodal	Mean thickness of rostralanteriorcingulate R	1.59 ± 0.25	2.29 ± 0.37	23.00	-1.877	0.007	0.073

Multimodal	Mean thickness of rostralmiddlefrontal L	1.64 ± 0.13	2.08 ± 0.19	13.00	-2.324	0.003	0.073
Multimodal	Mean thickness of rostralmiddlefrontal R	1.60 ± 0.04	2.06 ± 0.17	2.00	-2.791	0.001	0.073
Multimodal	Mean thickness of superiorfrontal L	1.94 ± 0.12	2.33 ± 0.22	24.00	-1.794	0.008	0.074
Multimodal	Mean thickness of superiorfrontal R	1.89 ± 0.03	2.30 ± 0.24	25.00	-1.736	0.008	0.076
Multimodal	Mean thickness of superiorparietal L	1.62 ± 0.09	1.99 ± 0.22	27.00	-1.679	0.010	0.078
Multimodal	Mean thickness of superiorparietal R	1.66 ± 0.07	1.97 ± 0.22	29.00	-1.430	0.012	0.082
Multimodal	Mean thickness of superiortemporal L	1.67 ± 0.21	2.41 ± 0.38	20.00	-1.980	0.006	0.073
Multimodal	Mean thickness of superiortemporal R	1.63 ± 0.13	2.42 ± 0.40	23.00	-2.009	0.007	0.073
Multimodal	Mean thickness of supramarginal L	1.46 ± 0.05	2.17 ± 0.35	25.50	-2.049	0.009	0.077
Multimodal	Mean thickness of supramarginal R	1.42 ± 0.08	2.13 ± 0.37	30.00	-1.918	0.012	0.083
Multimodal	Mean thickness of transversetemporal L	1.25 ± 0.11	2.09 ± 0.45	21.00	-1.875	0.006	0.073
Multimodal	Mean thickness of transversetemporal R	1.69 ± 0.32	2.14 ± 0.43	51.00	-1.038	0.054	0.207
Multimodal	Volume of caudalanteriorcingulate L	1595.75 ± 343.68	2320.18 ± 637.76	31.00	-1.142	0.013	0.084
Multimodal	Volume of caudalanteriorcingulate R	1098.50 ± 279.50	1722.70 ± 530.61	30.00	-1.183	0.012	0.083
Multimodal	Volume of caudalmiddlefrontal L	4923.50 ± 1065.79	5637.56 ± 1058.14	66.00	-0.667	0.130	0.399
Multimodal	Volume of caudalmiddlefrontal R	5163.75 ± 1084.91	5165.90 ± 1293.04	128.00	-0.002	0.881	0.951
Multimodal	Volume of cuneus L	1815.25 ± 534.66	3651.89 ± 1292.50	34.00	-1.433	0.017	0.094
Multimodal	Volume of cuneus R	1845.25 ± 381.30	3628.67 ± 1348.95	-2.62	-1.336	0.011	0.082
Multimodal	Volume of entorhinal L	1678.00 ± 245.11	1559.95 ± 359.67	0.64	0.329	0.522	0.845
Multimodal	Volume of entorhinal R	1540.50 ± 166.13	1551.31 ± 335.60	-0.06	-0.032	0.950	0.981
Multimodal	Volume of fusiform L	4063.50 ± 995.21	6805.82 ± 1916.66	27.00	-1.439	0.010	0.078
Multimodal	Volume of fusiform R	4305.50 ± 1290.35	6650.02 ± 2103.22	45.00	-1.118	0.037	0.155
Multimodal	Volume of inferiorparietal L	5617.25 ± 712.41	9802.03 ± 2463.50	-3.37	-1.716	0.001	0.073
Multimodal	Volume of inferiorparietal R	6465.75 ± 850.79	11498.18 ± 2959.55	-3.37	-1.718	0.001	0.073
Multimodal	Volume of inferiortemporal L	6051.50 ± 1151.37	9733.87 ± 2246.84	-3.23	-1.649	0.002	0.073
Multimodal	Volume of inferiortemporal R	6138.00 ± 458.09	9804.87 ± 2449.12	-2.97	-1.515	0.004	0.073
Multimodal	Volume of insula L	2141.50 ± 313.00	4781.03 ± 1490.74	33.00	-1.791	0.016	0.090
Multimodal	Volume of insula R	2041.50 ± 362.09	4969.66 ± 1426.35	22.00	-2.075	0.007	0.073
Multimodal	Volume of isthmuscingulate L	893.75 ± 542.41	2168.16 ± 626.52	17.00	-2.022	0.004	0.073
Multimodal	Volume of isthmuscingulate R	556.75 ± 490.85	1985.77 ± 658.40	17.00	-2.168	0.004	0.073
Multimodal	Volume of lateraloccipital L	7020.25 ± 1483.92	10465.49 ± 2416.02	27.00	-1.430	0.010	0.078
Multimodal	Volume of lateraloccipital R	6925.75 ± 1422.73	10838.03 ± 2709.78	31.00	-1.452	0.013	0.084
Multimodal	Volume of lateralorbitofrontal L	4990.25 ± 707.57	7276.16 ± 1487.67	27.00	-1.547	0.010	0.078
Multimodal	Volume of lateralorbitofrontal R	4850.25 ± 635.22	6997.02 ± 1456.36	28.00	-1.485	0.011	0.082
Multimodal	Volume of lingual L	3127.50 ± 471.59	5988.36 ± 1898.84	35.00	-1.523	0.018	0.096

Multimodal	Volume of lingual R	2674.75 ± 616.54	6210.43 ± 2038.16	21.00	-1.752	0.006	0.073
Multimodal	Volume of medialorbitofrontal L	3051.00 ± 277.66	3890.59 ± 778.19	41.00	-1.089	0.028	0.125
Multimodal	Volume of medialorbitofrontal R	2447.75 ± 468.92	3831.52 ± 796.75	18.00	-1.743	0.005	0.073
Multimodal	Volume of middletemporal L	6164.25 ± 982.81	10893.18 ± 2904.93	29.00	-1.643	0.012	0.082
Multimodal	Volume of middletemporal R	6179.25 ± 738.50	10780.80 ± 2964.62	33.00	-1.569	0.016	0.090
Multimodal	Volume of paracentral L	3412.50 ± 678.01	3655.25 ± 665.47	-0.71	-0.360	0.483	0.819
Multimodal	Volume of paracentral R	3398.50 ± 271.79	3500.48 ± 773.32	-0.26	-0.133	0.795	0.919
Multimodal	Volume of parahippocampal L	1645.50 ± 826.76	1864.03 ± 466.04	79.00	-0.441	0.246	0.575
Multimodal	Volume of parahippocampal R	1450.50 ± 495.37	1742.95 ± 458.42	74.00	-0.628	0.195	0.520
Multimodal	Volume of parsopercularis L	2151.50 ± 330.67	3201.20 ± 682.18	-3.04	-1.549	0.003	0.073
Multimodal	Volume of parsopercularis R	2354.50 ± 610.84	3346.07 ± 890.49	40.00	-1.114	0.026	0.117
Multimodal	Volume of parsorbitalis L	1241.50 ± 207.93	1763.92 ± 400.39	29.00	-1.312	0.012	0.082
Multimodal	Volume of parsorbitalis R	1188.75 ± 165.44	1806.46 ± 442.72	30.00	-1.408	0.012	0.083
Multimodal	Volume of parstriangularis L	2674.25 ± 884.85	3372.87 ± 648.18	-2.05	-1.044	0.045	0.179
Multimodal	Volume of parstriangularis R	2676.25 ± 159.71	3218.82 ± 759.45	-1.42	-0.723	0.161	0.457
Multimodal	Volume of pericalcarine L	1131.75 ± 166.97	1770.56 ± 549.88	-2.30	-1.173	0.025	0.114
Multimodal	Volume of pericalcarine R	1361.00 ± 153.18	1992.80 ± 662.82	-1.89	-0.964	0.063	0.235
Multimodal	Volume of postcentral L	9468.25 ± 1715.30	9204.82 ± 1374.33	0.37	0.187	0.715	0.908
Multimodal	Volume of postcentral R	8334.00 ± 1364.51	8610.82 ± 1531.09	-0.35	-0.180	0.726	0.908
Multimodal	Volume of posteriorcingulate L	1492.00 ± 319.65	2561.61 ± 785.16	31.00	-1.374	0.013	0.084
Multimodal	Volume of posteriorcingulate R	1218.00 ± 304.47	2595.82 ± 814.17	27.00	-1.707	0.010	0.078
Multimodal	Volume of precentral L	8986.75 ± 1550.61	11057.39 ± 2263.45	51.00	-0.916	0.054	0.207
Multimodal	Volume of precentral R	7653.75 ± 1367.85	10586.16 ± 2295.63	36.00	-1.282	0.020	0.096
Multimodal	Volume of precuneus L	5312.50 ± 825.43	7794.69 ± 2109.33	39.00	-1.187	0.024	0.113
Multimodal	Volume of precuneus R	4783.75 ± 549.09	8068.80 ± 2251.30	36.00	-1.475	0.020	0.096
Multimodal	Volume of rostralanteriorcingulate L	2131.25 ± 718.38	2577.05 ± 736.83	79.00	-0.598	0.246	0.575
Multimodal	Volume of rostralanteriorcingulate R	1251.50 ± 119.17	1939.79 ± 580.95	-2.35	-1.198	0.022	0.105
Multimodal	Volume of rostralmiddlefrontal L	8782.25 ± 565.40	8721.25 ± 1494.07	137.00	0.041	0.692	0.906
Multimodal	Volume of rostralmiddlefrontal R	8506.00 ± 1619.53	8846.10 ± 1765.59	-0.37	-0.191	0.709	0.908
Multimodal	Volume of superiorfrontal L	19867.50 ± 4116.60	20417.28 ± 2735.32	-0.38	-0.193	0.707	0.908
Multimodal	Volume of superiorfrontal R	22531.50 ± 4123.45	22391.13 ± 3015.63	0.09	0.045	0.930	0.972
Multimodal	Volume of superiorparietal L	7339.75 ± 1253.77	8987.23 ± 1543.32	-2.09	-1.063	0.041	0.168
Multimodal	Volume of superiorparietal R	8355.75 ± 1384.80	8938.64 ± 1694.33	-0.67	-0.343	0.504	0.836
Multimodal	Volume of superiortemporal L	8308.75 ± 1626.28	13088.57 ± 3445.57	33.00	-1.397	0.016	0.090
Multimodal	Volume of superiortemporal R	6720.00 ± 1387.50	12474.03 ± 3241.35	25.00	-1.789	0.008	0.076

Multimodal	Volume of supramarginal L	5272.75 ± 1310.01	8061.90 ± 2161.68	36.00	-1.294	0.020	0.096
Multimodal	Volume of supramarginal R	5225.75 ± 1564.54	7428.20 ± 2169.73	-1.99	-1.015	0.051	0.197
Multimodal	Volume of transversetemporal L	465.50 ± 215.69	896.72 ± 331.23	36.00	-1.304	0.020	0.096
Multimodal	Volume of transversetemporal R	353.75 ± 180.51	711.64 ± 264.06	32.00	-1.356	0.015	0.088
Multimodal	Volume of accumbens L	774.50 ± 185.30	662.70 ± 147.02	1.45	0.741	0.151	0.434
Multimodal	Volume of accumbens R	623.25 ± 108.84	544.70 ± 135.88	1.13	0.576	0.263	0.604
Multimodal	Volume of amygdala L	1144.00 ± 530.27	1527.25 ± 389.49	61.00	-0.953	0.099	0.322
Multimodal	Volume of amygdala R	1524.50 ± 576.03	1615.75 ± 340.63	-0.50	-0.254	0.621	0.875
Multimodal	Volume of caudate L	4070.75 ± 617.53	4106.10 ± 558.64	-0.12	-0.062	0.903	0.964
Multimodal	Volume of caudate R	4679.25 ± 483.39	4544.44 ± 501.62	0.52	0.266	0.604	0.870
Multimodal	Volume of hippocampus L	5131.50 ± 377.61	5041.31 ± 569.87	130.50	0.159	0.827	0.934
Multimodal	Volume of hippocampus R	5881.25 ± 595.55	5296.34 ± 609.38	1.86	0.949	0.067	0.243
Multimodal	Volume of pallidum L	2110.00 ± 285.99	2129.20 ± 374.07	121.00	-0.051	0.989	0.993
Multimodal	Volume of pallidum R	2347.50 ± 212.96	2146.10 ± 368.41	1.08	0.549	0.286	0.624
Multimodal	Volume of putamen L	7313.25 ± 367.03	6663.90 ± 618.40	2.07	1.054	0.043	0.172
Multimodal	Volume of putamen R	6692.75 ± 290.48	6341.20 ± 660.00	1.05	0.537	0.297	0.639
Multimodal	Volume of thalamus L	9709.50 ± 918.98	9229.66 ± 976.88	170.00	0.487	0.195	0.520
Multimodal	Volume of thalamus R	9250.00 ± 1156.13	9051.59 ± 709.66	142.00	0.266	0.595	0.866
Multimodal	Mean FA in anterior corona radiata L	0.44 ± 0.03	0.42 ± 0.02	1.58	0.806	0.119	0.372
Multimodal	Mean FA in anterior corona radiata R	0.44 ± 0.03	0.42 ± 0.03	1.25	0.635	0.218	0.549
Multimodal	Mean FA in anterior limb of internal capsule L	0.57 ± 0.04	0.56 ± 0.03	0.60	0.305	0.552	0.859
Multimodal	Mean FA in anterior limb of internal capsule R	0.57 ± 0.04	0.56 ± 0.03	0.46	0.237	0.644	0.878
Multimodal	Mean FA in body of corpus callosum	0.68 ± 0.03	0.67 ± 0.03	0.77	0.394	0.443	0.789
Multimodal	Mean FA in cerebral peduncle L	0.70 ± 0.06	0.69 ± 0.02	171.00	0.441	0.186	0.500
Multimodal	Mean FA in cerebral peduncle R	0.68 ± 0.04	0.69 ± 0.03	-0.51	-0.260	0.612	0.872
Multimodal	Mean FA in cingulum cingulate gyrus L	0.58 ± 0.02	0.57 ± 0.03	0.53	0.269	0.599	0.869
Multimodal	Mean FA in cingulum cingulate gyrus R	0.53 ± 0.02	0.53 ± 0.03	0.47	0.241	0.638	0.878
Multimodal	Mean FA in cingulum hippocampus L	0.47 ± 0.05	0.48 ± 0.03	-0.25	-0.125	0.807	0.927
Multimodal	Mean FA in cingulum hippocampus R	0.43 ± 0.05	0.47 ± 0.03	-2.25	-1.145	0.028	0.125
Multimodal	Mean FA in corticospinal tract L	0.53 ± 0.07	0.54 ± 0.04	-0.40	-0.203	0.691	0.906
Multimodal	Mean FA in corticospinal tract R	0.49 ± 0.04	0.52 ± 0.03	-1.78	-0.906	0.080	0.276
Multimodal	Mean FA in external capsule L	0.43 ± 0.06	0.42 ± 0.03	161.00	0.200	0.293	0.635
Multimodal	Mean FA in external capsule R	0.42 ± 0.04	0.41 ± 0.02	0.58	0.297	0.563	0.860
Multimodal	Mean FA in fornix cres+stria terminalis L	0.56 ± 0.07	0.54 ± 0.04	164.00	0.553	0.257	0.594
Multimodal	Mean FA in fornix cres+stria terminalis R	0.53 ± 0.02	0.53 ± 0.03	127.00	0.041	0.902	0.964

Multimodal	Mean FA in fornix	0.53 ± 0.04	0.43 ± 0.06	3.01	1.535	0.004	0.073
Multimodal	Mean FA in genu of corpus callosum	0.69 ± 0.03	0.67 ± 0.03	162.00	0.540	0.281	0.618
Multimodal	Mean FA in inferior cerebellar peduncle L	0.53 ± 0.02	0.55 ± 0.03	-1.19	-0.608	0.238	0.566
Multimodal	Mean FA in inferior cerebellar peduncle R	0.55 ± 0.02	0.54 ± 0.02	0.56	0.288	0.575	0.860
Multimodal	Mean FA in medial lemniscus L	0.56 ± 0.03	0.57 ± 0.03	-0.38	-0.193	0.706	0.908
Multimodal	Mean FA in medial lemniscus R	0.58 ± 0.03	0.57 ± 0.03	0.74	0.378	0.461	0.806
Multimodal	Mean FA in middle cerebellar peduncle	0.54 ± 0.01	0.55 ± 0.02	-0.66	-0.338	0.510	0.841
Multimodal	Mean FA in pontine crossing tract	0.46 ± 0.05	0.47 ± 0.04	102.00	-0.238	0.595	0.866
Multimodal	Mean FA in posterior corona radiata L	0.45 ± 0.04	0.45 ± 0.03	0.17	0.089	0.863	0.948
Multimodal	Mean FA in posterior corona radiata R	0.47 ± 0.03	0.46 ± 0.02	0.32	0.163	0.750	0.919
Multimodal	Mean FA in posterior limb of internal capsule L	0.67 ± 0.06	0.67 ± 0.03	153.00	-0.004	0.405	0.760
Multimodal	Mean FA in posterior limb of internal capsule R	0.66 ± 0.06	0.66 ± 0.03	-0.27	-0.139	0.786	0.919
Multimodal	Mean FA in posterior thalamic radiation L	0.58 ± 0.03	0.58 ± 0.03	0.02	0.012	0.981	0.990
Multimodal	Mean FA in posterior thalamic radiation R	0.58 ± 0.03	0.57 ± 0.03	0.19	0.097	0.850	0.947
Multimodal	Mean FA in retrolenticular part of internal capsule L	0.60 ± 0.06	0.60 ± 0.03	0.05	0.026	0.960	0.984
Multimodal	Mean FA in retrolenticular part of internal capsule R	0.54 ± 0.04	0.56 ± 0.03	-1.34	-0.683	0.185	0.500
Multimodal	Mean FA in sagittal stratum L	0.55 ± 0.04	0.55 ± 0.03	-0.28	-0.143	0.780	0.919
Multimodal	Mean FA in sagittal stratum R	0.53 ± 0.03	0.55 ± 0.03	-1.23	-0.626	0.224	0.551
Multimodal	Mean FA in splenium of corpus callosum	0.76 ± 0.03	0.76 ± 0.03	-0.25	-0.126	0.805	0.927
Multimodal	Mean FA in superior cerebellar peduncle L	0.69 ± 0.05	0.67 ± 0.03	0.84	0.430	0.403	0.760
Multimodal	Mean FA in superior cerebellar peduncle R	0.69 ± 0.04	0.67 ± 0.03	1.28	0.652	0.206	0.527
Multimodal	Mean FA in superior corona radiata L	0.45 ± 0.04	0.46 ± 0.03	-0.74	-0.378	0.461	0.806
Multimodal	Mean FA in superior corona radiata R	0.45 ± 0.04	0.45 ± 0.03	0.03	0.017	0.973	0.987
Multimodal	Mean FA in superior fronto-occipital fasciculus L	0.45 ± 0.04	0.44 ± 0.04	0.71	0.364	0.478	0.814
Multimodal	Mean FA in superior fronto-occipital fasciculus R	0.44 ± 0.03	0.44 ± 0.03	0.19	0.096	0.851	0.947
Multimodal	Mean FA in superior longitudinal fasciculus L	0.50 ± 0.03	0.49 ± 0.03	136.00	0.134	0.712	0.908
Multimodal	Mean FA in superior longitudinal fasciculus R	0.47 ± 0.03	0.48 ± 0.03	97.00	-0.404	0.504	0.836
Multimodal	Mean FA in tapetum L	0.58 ± 0.09	0.58 ± 0.06	0.17	0.088	0.864	0.948
Multimodal	Mean FA in tapetum R	0.58 ± 0.09	0.55 ± 0.06	0.97	0.496	0.334	0.690
Multimodal	Mean FA in uncinate fasciculus L	0.50 ± 0.05	0.48 ± 0.04	0.52	0.264	0.606	0.870
Multimodal	Mean FA in uncinate fasciculus R	0.51 ± 0.07	0.50 ± 0.04	140.00	0.410	0.633	0.876
Multimodal	Mean AD in anterior corona radiata L	0.12 ± 0.01	0.12 ± 0.00	-0.65	-0.333	0.517	0.845
Multimodal	Mean AD in anterior corona radiata R	0.12 ± 0.01	0.12 ± 0.00	-0.77	-0.391	0.446	0.793
Multimodal	Mean AD in anterior limb of internal capsule L	0.12 ± 0.00	0.12 ± 0.00	-0.90	-0.457	0.373	0.728
Multimodal	Mean AD in anterior limb of internal capsule R	0.12 ± 0.00	0.13 ± 0.00	-0.66	-0.339	0.509	0.841
Multimodal	Mean AD in body of corpus callosum	0.16 ± 0.01	0.16 ± 0.00	-0.64	-0.324	0.528	0.849

Multimodal	Mean AD in cerebral peduncle L	0.14 ± 0.00	0.14 ± 0.01	-1.09	-0.556	0.279	0.618
Multimodal	Mean AD in cerebral peduncle R	0.14 ± 0.00	0.14 ± 0.01	-0.83	-0.426	0.407	0.760
Multimodal	Mean AD in cingulum cingulate gyrus L	0.13 ± 0.00	0.13 ± 0.01	0.63	0.319	0.534	0.849
Multimodal	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.00	0.13 ± 0.01	0.44	0.226	0.659	0.885
Multimodal	Mean AD in cingulum hippocampus L	0.12 ± 0.01	0.12 ± 0.01	-0.48	-0.245	0.632	0.876
Multimodal	Mean AD in cingulum hippocampus R	0.12 ± 0.01	0.13 ± 0.01	75.00	-0.603	0.204	0.527
Multimodal	Mean AD in corticospinal tract L	0.12 ± 0.01	0.12 ± 0.01	0.33	0.169	0.741	0.915
Multimodal	Mean AD in corticospinal tract R	0.12 ± 0.01	0.12 ± 0.01	0.35	0.180	0.726	0.908
Multimodal	Mean AD in external capsule L	0.11 ± 0.00	0.11 ± 0.00	-0.62	-0.318	0.535	0.849
Multimodal	Mean AD in external capsule R	0.11 ± 0.00	0.11 ± 0.00	-0.58	-0.293	0.567	0.860
Multimodal	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.00	0.13 ± 0.01	150.00	0.411	0.453	0.802
Multimodal	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.00	0.14 ± 0.00	121.50	0.120	1.000	1.000
Multimodal	Mean AD in fornix	0.20 ± 0.02	0.23 ± 0.02	-2.03	-1.038	0.046	0.182
Multimodal	Mean AD in genu of corpus callosum	0.16 ± 0.01	0.16 ± 0.00	-0.81	-0.413	0.421	0.775
Multimodal	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.00	0.12 ± 0.01	-1.31	-0.667	0.196	0.520
Multimodal	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.00	0.12 ± 0.01	0.74	0.378	0.461	0.806
Multimodal	Mean AD in medial lemniscus L	0.13 ± 0.00	0.13 ± 0.01	0.47	0.238	0.642	0.878
Multimodal	Mean AD in medial lemniscus R	0.13 ± 0.00	0.13 ± 0.01	0.45	0.229	0.654	0.883
Multimodal	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	99.00	-0.357	0.539	0.849
Multimodal	Mean AD in pontine crossing tract	0.11 ± 0.01	0.11 ± 0.01	0.91	0.465	0.365	0.722
Multimodal	Mean AD in posterior corona radiata L	0.12 ± 0.00	0.12 ± 0.01	57.00	-0.726	0.078	0.271
Multimodal	Mean AD in posterior corona radiata R	0.12 ± 0.00	0.13 ± 0.01	-1.62	-0.828	0.109	0.348
Multimodal	Mean AD in posterior limb of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	-0.17	-0.087	0.864	0.948
Multimodal	Mean AD in posterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	-0.99	-0.504	0.327	0.678
Multimodal	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	-0.65	-0.333	0.516	0.845
Multimodal	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.01	-0.27	-0.138	0.788	0.919
Multimodal	Mean AD in retrolenticular part of internal capsule L	0.13 ± 0.00	0.13 ± 0.00	-1.63	-0.832	0.108	0.348
Multimodal	Mean AD in retrolenticular part of internal capsule R	0.13 ± 0.01	0.14 ± 0.00	-3.44	-1.756	0.001	0.073
Multimodal	Mean AD in sagittal stratum L	0.13 ± 0.00	0.14 ± 0.01	-2.11	-1.078	0.038	0.160
Multimodal	Mean AD in sagittal stratum R	0.13 ± 0.01	0.14 ± 0.01	-1.76	-0.898	0.083	0.284
Multimodal	Mean AD in splenium of corpus callosum	0.16 ± 0.00	0.16 ± 0.01	-1.63	-0.834	0.107	0.348
Multimodal	Mean AD in superior cerebellar peduncle L	0.15 ± 0.01	0.16 ± 0.01	-0.53	-0.268	0.601	0.869
Multimodal	Mean AD in superior cerebellar peduncle R	0.15 ± 0.01	0.16 ± 0.01	-1.28	-0.653	0.205	0.527
Multimodal	Mean AD in superior corona radiata L	0.11 ± 0.00	0.11 ± 0.00	-1.35	-0.687	0.183	0.500
Multimodal	Mean AD in superior corona radiata R	0.11 ± 0.00	0.11 ± 0.00	-0.75	-0.380	0.458	0.806

Multimodal	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.00	0.11 ± 0.01	-0.50	-0.254	0.621	0.875
Multimodal	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.11 ± 0.01	0.21	0.108	0.833	0.939
Multimodal	Mean AD in superior longitudinal fasciculus L	0.11 ± 0.00	0.12 ± 0.00	-0.55	-0.281	0.584	0.864
Multimodal	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	-1.19	-0.609	0.237	0.566
Multimodal	Mean AD in tapetum L	0.16 ± 0.00	0.16 ± 0.01	113.50	-0.076	0.827	0.934
Multimodal	Mean AD in tapetum R	0.17 ± 0.00	0.17 ± 0.01	0.11	0.056	0.913	0.968
Multimodal	Mean AD in uncinate fasciculus L	0.13 ± 0.00	0.13 ± 0.01	-0.47	-0.238	0.642	0.878
Multimodal	Mean AD in uncinate fasciculus R	0.13 ± 0.01	0.13 ± 0.01	167.50	0.597	0.219	0.549
Multimodal	Mean RD in anterior corona radiata L	0.06 ± 0.01	0.06 ± 0.00	-1.50	-0.766	0.138	0.418
Multimodal	Mean RD in anterior corona radiata R	0.06 ± 0.01	0.06 ± 0.00	-1.45	-0.741	0.151	0.434
Multimodal	Mean RD in anterior limb of internal capsule L	0.04 ± 0.00	0.05 ± 0.00	81.00	-0.409	0.269	0.610
Multimodal	Mean RD in anterior limb of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	-0.56	-0.287	0.575	0.860
Multimodal	Mean RD in body of corpus callosum	0.04 ± 0.00	0.04 ± 0.00	-0.78	-0.400	0.436	0.781
Multimodal	Mean RD in cerebral peduncle L	0.04 ± 0.01	0.04 ± 0.00	70.00	-0.613	0.160	0.454
Multimodal	Mean RD in cerebral peduncle R	0.04 ± 0.01	0.04 ± 0.00	0.23	0.120	0.815	0.930
Multimodal	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.05 ± 0.00	-0.34	-0.174	0.734	0.908
Multimodal	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.05 ± 0.00	-0.23	-0.116	0.821	0.933
Multimodal	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.06 ± 0.00	-0.40	-0.206	0.688	0.906
Multimodal	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.06 ± 0.00	1.19	0.608	0.238	0.566
Multimodal	Mean RD in corticospinal tract L	0.05 ± 0.01	0.05 ± 0.00	160.50	0.226	0.300	0.643
Multimodal	Mean RD in corticospinal tract R	0.05 ± 0.00	0.05 ± 0.00	1.95	0.994	0.056	0.211
Multimodal	Mean RD in external capsule L	0.06 ± 0.01	0.06 ± 0.00	77.00	-0.331	0.224	0.551
Multimodal	Mean RD in external capsule R	0.06 ± 0.01	0.06 ± 0.00	76.50	-0.402	0.219	0.549
Multimodal	Mean RD in fornix cres+stria terminalis L	0.05 ± 0.01	0.05 ± 0.00	-0.78	-0.400	0.436	0.781
Multimodal	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.00	0.06 ± 0.00	109.00	-0.162	0.733	0.908
Multimodal	Mean RD in fornix	0.09 ± 0.01	0.12 ± 0.03	30.00	-1.250	0.012	0.083
Multimodal	Mean RD in genu of corpus callosum	0.04 ± 0.00	0.04 ± 0.00	-1.22	-0.624	0.226	0.551
Multimodal	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	0.05	0.025	0.961	0.984
Multimodal	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	-0.37	-0.187	0.715	0.908
Multimodal	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	0.72	0.366	0.476	0.813
Multimodal	Mean RD in medial lemniscus R	0.05 ± 0.00	0.05 ± 0.00	-0.42	-0.215	0.674	0.902
Multimodal	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	0.17	0.084	0.869	0.950
Multimodal	Mean RD in pontine crossing tract	0.05 ± 0.00	0.05 ± 0.00	0.89	0.453	0.377	0.730
Multimodal	Mean RD in posterior corona radiata L	0.06 ± 0.01	0.06 ± 0.00	-0.60	-0.304	0.553	0.859
Multimodal	Mean RD in posterior corona radiata R	0.06 ± 0.01	0.06 ± 0.00	-0.68	-0.345	0.502	0.836
Multimodal	Mean RD in posterior limb of internal capsule L	0.04 ± 0.01	0.04 ± 0.00	85.50	-0.006	0.326	0.678

Multimodal	Mean RD in posterior limb of internal capsule R	0.04 ± 0.01	0.04 ± 0.00	-0.03	-0.015	0.976	0.987
Multimodal	Mean RD in posterior thalamic radiation L	0.05 ± 0.01	0.05 ± 0.01	-0.37	-0.188	0.714	0.908
Multimodal	Mean RD in posterior thalamic radiation R	0.05 ± 0.01	0.05 ± 0.00	-0.40	-0.204	0.690	0.906
Multimodal	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.01	0.05 ± 0.00	-0.62	-0.316	0.537	0.849
Multimodal	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.01	0.05 ± 0.00	0.13	0.066	0.897	0.964
Multimodal	Mean RD in sagittal stratum L	0.05 ± 0.00	0.05 ± 0.00	-0.61	-0.311	0.544	0.852
Multimodal	Mean RD in sagittal stratum R	0.06 ± 0.00	0.06 ± 0.00	0.17	0.089	0.862	0.948
Multimodal	Mean RD in splenium of corpus callosum	0.03 ± 0.00	0.03 ± 0.00	-0.13	-0.065	0.899	0.964
Multimodal	Mean RD in superior cerebellar peduncle L	0.04 ± 0.01	0.04 ± 0.00	-1.29	-0.657	0.202	0.527
Multimodal	Mean RD in superior cerebellar peduncle R	0.04 ± 0.00	0.05 ± 0.00	-2.09	-1.068	0.040	0.167
Multimodal	Mean RD in superior corona radiata L	0.05 ± 0.01	0.05 ± 0.00	0.35	0.179	0.727	0.908
Multimodal	Mean RD in superior corona radiata R	0.05 ± 0.01	0.05 ± 0.00	-0.26	-0.135	0.792	0.919
Multimodal	Mean RD in superior fronto-occipital fasciculus L	0.05 ± 0.00	0.05 ± 0.00	77.00	-0.535	0.224	0.551
Multimodal	Mean RD in superior fronto-occipital fasciculus R	0.05 ± 0.00	0.06 ± 0.00	111.50	-0.035	0.785	0.919
Multimodal	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.01	0.05 ± 0.00	101.50	-0.098	0.585	0.864
Multimodal	Mean RD in superior longitudinal fasciculus R	0.05 ± 0.01	0.05 ± 0.00	0.16	0.080	0.876	0.951
Multimodal	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	-0.10	-0.052	0.920	0.972
Multimodal	Mean RD in tapetum R	0.06 ± 0.01	0.07 ± 0.01	-0.73	-0.371	0.470	0.813
Multimodal	Mean RD in uncinate fasciculus L	0.05 ± 0.01	0.06 ± 0.00	-1.03	-0.526	0.306	0.649
Multimodal	Mean RD in uncinate fasciculus R	0.06 ± 0.01	0.06 ± 0.00	-0.11	-0.054	0.916	0.970
Multimodal	Spos_1	7.44 ± 6.38	6.81 ± 3.49	109.00	0.169	0.733	0.908
Multimodal	Spos_2	16.25 ± 6.20	11.80 ± 4.89	1.74	0.887	0.087	0.294
Multimodal	Spos_3	7.57 ± 0.53	9.12 ± 4.84	87.00	-0.325	0.346	0.702
Multimodal	Spos_4	12.15 ± 6.25	9.78 ± 4.61	156.00	0.497	0.360	0.716
Multimodal	Spos_5	6.63 ± 2.99	16.17 ± 6.94	-2.72	-1.386	0.008	0.076
Multimodal	Spos_6	4.34 ± 2.56	4.79 ± 3.05	116.00	-0.146	0.881	0.951
Multimodal	Spos_7	14.16 ± 7.47	12.69 ± 5.47	151.00	0.260	0.437	0.781
Multimodal	Spos_8	7.03 ± 1.34	8.47 ± 4.57	107.00	-0.319	0.692	0.906
Multimodal	Spos_9	7.69 ± 5.10	10.63 ± 4.84	-1.17	-0.597	0.246	0.575
Multimodal	Spos_10	14.99 ± 3.48	11.86 ± 6.14	163.00	0.512	0.269	0.610
Multimodal	Spos_11	14.92 ± 6.92	16.45 ± 5.86	98.00	-0.256	0.521	0.845
Multimodal	Spos_12	17.24 ± 7.84	13.62 ± 6.23	1.11	0.566	0.271	0.613
Multimodal	Spos_13	11.08 ± 5.31	11.90 ± 6.15	111.00	-0.131	0.774	0.919
Multimodal	Spos_14	9.05 ± 1.14	10.75 ± 5.43	102.00	-0.318	0.595	0.866
Multimodal	Spos_15	11.77 ± 3.06	12.72 ± 6.53	124.00	-0.146	0.967	0.984
Multimodal	Spos_16	3.21 ± 1.25	3.98 ± 2.17	104.00	-0.357	0.633	0.876
Multimodal	Spos_17	9.29 ± 6.09	10.85 ± 4.81	-0.62	-0.317	0.537	0.849
Multimodal	Spos_18	8.33 ± 3.30	10.80 ± 4.78	-1.01	-0.515	0.316	0.668
Multimodal	Spos_19	9.09 ± 3.97	10.98 ± 5.38	-0.69	-0.350	0.495	0.834
Multimodal	Spos_20	5.27 ± 1.91	5.59 ± 2.15	-0.29	-0.147	0.774	0.919

Multimodal	Spos_21	13.20 ± 4.36	11.83 ± 5.33	0.50	0.256	0.617	0.875
Multimodal	Spos_22	11.60 ± 5.71	8.48 ± 3.93	165.00	0.765	0.246	0.575
Multimodal	Spos_23	14.44 ± 6.84	13.15 ± 5.92	0.42	0.214	0.676	0.903
Multimodal	Spos_24	14.99 ± 3.58	15.52 ± 7.83	120.00	-0.068	0.967	0.984
Multimodal	Spos_25	12.66 ± 4.81	11.21 ± 5.04	0.56	0.285	0.579	0.862
Multimodal	Spos_26	10.63 ± 5.17	10.22 ± 4.61	0.17	0.087	0.865	0.948
Multimodal	Spos_27	11.41 ± 6.77	11.56 ± 5.39	111.00	-0.027	0.774	0.919
Multimodal	Spos_28	8.43 ± 2.64	9.76 ± 5.25	108.00	-0.256	0.712	0.908
Multimodal	Spos_29	11.09 ± 3.70	11.38 ± 5.23	126.00	-0.055	0.924	0.972
Multimodal	Spos_30	6.10 ± 2.32	6.73 ± 3.32	111.00	-0.190	0.774	0.919
Multimodal	Spos_31	9.55 ± 6.96	11.63 ± 5.28	87.00	-0.383	0.346	0.702
Multimodal	Spos_32	9.55 ± 4.64	6.41 ± 3.30	168.00	0.917	0.214	0.544
Multimodal	Spos_33	10.16 ± 5.25	9.59 ± 4.51	0.24	0.123	0.810	0.928
Multimodal	Spos_34	11.04 ± 5.38	10.81 ± 4.34	131.00	0.053	0.817	0.930
Multimodal	Spos_35	8.03 ± 6.14	8.62 ± 3.70	-0.29	-0.150	0.770	0.919
Multimodal	Spos_36	19.25 ± 12.04	15.85 ± 6.24	148.00	0.505	0.486	0.823
Multimodal	Spos_37	9.01 ± 3.59	12.12 ± 5.51	82.00	-0.566	0.281	0.618
Multimodal	Spos_38	9.87 ± 2.94	10.15 ± 4.82	125.00	-0.059	0.946	0.979
Multimodal	Spos_39	22.67 ± 4.05	16.59 ± 8.01	189.00	0.764	0.069	0.249
Multimodal	Spos_40	9.34 ± 8.20	12.09 ± 5.79	93.00	-0.458	0.437	0.781
Multimodal	Spos_41	9.71 ± 2.05	9.20 ± 3.80	0.27	0.137	0.789	0.919
Multimodal	Spos_42	18.92 ± 6.34	12.76 ± 5.48	2.16	1.102	0.035	0.147
Multimodal	Spos_43	9.12 ± 6.94	10.22 ± 6.05	103.00	-0.179	0.614	0.872
Multimodal	Spos_44	12.17 ± 7.35	10.02 ± 5.14	0.79	0.404	0.431	0.781
Multimodal	Spos_45	7.23 ± 5.64	10.56 ± 4.81	82.00	-0.676	0.281	0.618
Multimodal	Spos_46	11.52 ± 8.07	11.17 ± 5.89	112.00	0.058	0.795	0.919
Multimodal	Spos_47	9.60 ± 4.08	9.94 ± 5.19	119.00	-0.066	0.946	0.979
Multimodal	Spos_48	12.83 ± 6.69	10.26 ± 5.14	0.95	0.486	0.344	0.702
Multimodal	Spos_49	11.13 ± 2.26	12.87 ± 5.87	110.00	-0.300	0.754	0.919
Multimodal	Spos_50	12.92 ± 10.29	11.90 ± 6.03	121.00	0.161	0.989	0.993
Multimodal	Spos_51	13.87 ± 1.77	11.40 ± 5.54	0.88	0.449	0.382	0.736
Multimodal	Spos_52	14.69 ± 4.34	9.54 ± 4.29	2.33	1.187	0.023	0.110
Multimodal	Spos_53	9.12 ± 8.75	9.84 ± 4.66	-0.28	-0.145	0.777	0.919
Multimodal	Spos_54	11.55 ± 8.16	8.45 ± 4.07	151.00	0.704	0.437	0.781
Multimodal	Spos_55	3.48 ± 1.19	5.15 ± 2.57	-1.28	-0.652	0.206	0.527
Multimodal	Sneg_1	6.51 ± 2.74	7.75 ± 4.09	107.00	-0.305	0.692	0.906
Multimodal	Sneg_2	13.79 ± 5.53	13.16 ± 6.33	134.00	0.099	0.754	0.919
Multimodal	Sneg_3	10.02 ± 3.06	8.69 ± 4.76	154.00	0.280	0.390	0.748
Multimodal	Sneg_4	7.74 ± 2.84	9.62 ± 4.45	91.00	-0.423	0.405	0.760
Multimodal	Sneg_5	4.43 ± 1.32	15.61 ± 6.96	6.00	-1.626	0.002	0.073
Multimodal	Sneg_6	5.13 ± 3.07	5.73 ± 3.90	116.00	-0.153	0.881	0.951
Multimodal	Sneg_7	15.90 ± 10.97	14.52 ± 6.56	0.39	0.200	0.697	0.908
Multimodal	Sneg_8	10.18 ± 2.84	9.22 ± 5.72	152.00	0.170	0.421	0.775
Multimodal	Sneg_9	7.94 ± 2.47	10.12 ± 5.03	-0.86	-0.437	0.395	0.756

Multimodal	Sneg_10	12.52 ± 4.10	12.07 ± 6.23	132.00	0.072	0.795	0.919
Multimodal	Sneg_11	16.28 ± 6.60	14.44 ± 5.46	0.65	0.331	0.519	0.845
Multimodal	Sneg_12	18.76 ± 6.97	13.36 ± 5.78	1.79	0.914	0.078	0.271
Multimodal	Sneg_13	9.72 ± 3.83	11.45 ± 5.03	100.00	-0.342	0.557	0.859
Multimodal	Sneg_14	12.12 ± 3.93	12.11 ± 6.83	133.00	0.001	0.774	0.919
Multimodal	Sneg_15	11.28 ± 5.05	13.50 ± 6.57	101.00	-0.337	0.576	0.860
Multimodal	Sneg_16	3.30 ± 1.93	4.06 ± 2.44	103.00	-0.309	0.614	0.872
Multimodal	Sneg_17	10.96 ± 4.75	10.50 ± 5.14	134.00	0.089	0.754	0.919
Multimodal	Sneg_18	9.93 ± 7.88	11.21 ± 5.53	89.00	-0.223	0.375	0.728
Multimodal	Sneg_19	7.79 ± 2.41	10.68 ± 5.50	-1.04	-0.530	0.303	0.645
Multimodal	Sneg_20	8.18 ± 3.82	6.71 ± 3.14	0.90	0.457	0.374	0.728
Multimodal	Sneg_21	7.91 ± 3.33	11.59 ± 5.01	-1.44	-0.735	0.154	0.441
Multimodal	Sneg_22	8.73 ± 3.99	8.49 ± 3.96	137.00	0.059	0.692	0.906
Multimodal	Sneg_23	12.11 ± 5.13	14.43 ± 6.18	-0.73	-0.373	0.467	0.811
Multimodal	Sneg_24	9.27 ± 1.76	13.19 ± 6.14	75.00	-0.644	0.204	0.527
Multimodal	Sneg_25	14.36 ± 5.43	11.30 ± 5.67	166.00	0.535	0.235	0.566
Multimodal	Sneg_26	9.19 ± 2.41	10.64 ± 4.89	-0.58	-0.297	0.562	0.860
Multimodal	Sneg_27	10.35 ± 5.03	12.62 ± 6.15	-0.72	-0.367	0.475	0.813
Multimodal	Sneg_28	9.74 ± 5.20	10.00 ± 5.73	126.00	-0.046	0.924	0.972
Multimodal	Sneg_29	11.40 ± 5.15	10.23 ± 4.41	137.00	0.260	0.692	0.906
Multimodal	Sneg_30	8.24 ± 8.46	7.41 ± 3.72	97.00	0.202	0.504	0.836
Multimodal	Sneg_31	8.29 ± 4.51	11.45 ± 5.28	88.00	-0.594	0.360	0.716
Multimodal	Sneg_32	9.56 ± 2.62	7.23 ± 3.81	177.00	0.612	0.137	0.418
Multimodal	Sneg_33	7.92 ± 1.92	9.40 ± 4.63	109.00	-0.323	0.733	0.908
Multimodal	Sneg_34	15.24 ± 7.49	11.59 ± 4.51	1.50	0.767	0.138	0.418
Multimodal	Sneg_35	9.62 ± 3.02	10.25 ± 4.64	-0.27	-0.136	0.791	0.919
Multimodal	Sneg_36	12.86 ± 7.37	14.03 ± 5.76	119.00	-0.198	0.946	0.979
Multimodal	Sneg_37	10.65 ± 6.53	12.41 ± 5.73	-0.59	-0.301	0.557	0.859
Multimodal	Sneg_38	6.46 ± 2.13	10.41 ± 4.53	-1.72	-0.877	0.091	0.305
Multimodal	Sneg_39	16.42 ± 5.86	14.70 ± 6.03	0.55	0.283	0.581	0.864
Multimodal	Sneg_40	10.10 ± 5.15	12.59 ± 6.05	99.00	-0.409	0.539	0.849
Multimodal	Sneg_41	6.94 ± 2.22	9.57 ± 5.07	85.00	-0.523	0.319	0.669
Multimodal	Sneg_42	14.30 ± 6.05	12.36 ± 5.24	159.00	0.364	0.319	0.669
Multimodal	Sneg_43	9.58 ± 4.72	11.16 ± 6.88	117.00	-0.229	0.902	0.964
Multimodal	Sneg_44	12.91 ± 3.90	9.55 ± 4.89	176.00	0.685	0.144	0.426
Multimodal	Sneg_45	7.59 ± 5.75	10.24 ± 4.12	-1.22	-0.623	0.226	0.551
Multimodal	Sneg_46	11.00 ± 6.29	10.91 ± 5.48	130.00	0.017	0.838	0.942
Multimodal	Sneg_47	9.23 ± 2.74	9.96 ± 5.09	120.00	-0.144	0.967	0.984
Multimodal	Sneg_48	11.79 ± 3.89	9.97 ± 5.27	163.00	0.345	0.269	0.610
Multimodal	Sneg_49	10.26 ± 2.85	10.74 ± 4.33	-0.22	-0.111	0.828	0.934
Multimodal	Sneg_50	13.62 ± 5.42	11.50 ± 6.14	157.00	0.343	0.346	0.702
Multimodal	Sneg_51	14.72 ± 2.17	11.22 ± 5.04	1.37	0.698	0.176	0.489
Multimodal	Sneg_52	12.37 ± 3.48	9.25 ± 4.08	1.50	0.762	0.140	0.418
Multimodal	Sneg_53	7.74 ± 5.00	9.34 ± 4.26	-0.72	-0.369	0.472	0.813

Multimodal	Sneg_54	13.24 ± 3.81	8.16 ± 4.04	2.44	1.246	0.017	0.095
Multimodal	Sneg_55	2.29 ± 0.19	5.06 ± 2.69	44.00	-1.045	0.034	0.147
Multimodal	Median z-statistic (amygdala) for faces-shapes contrast	1.32 ± 0.84	0.76 ± 0.72	1.50	0.764	0.139	0.418
Multimodal	Median z-statistic for faces activation	2.07 ± 0.34	2.08 ± 0.98	108.00	-0.010	0.712	0.908
Multimodal	Median z-statistic for shapes activation	1.56 ± 0.39	1.85 ± 0.92	-0.61	-0.313	0.541	0.849
Multimodal	Median z-statistic for faces-shapes contrast	3.26 ± 1.19	2.80 ± 1.71	0.53	0.268	0.601	0.869
Multimodal	90th percentile of z-statistic (amygdala) for faces-shapes	3.05 ± 1.12	2.30 ± 0.96	1.49	0.759	0.142	0.421
Multimodal	90th percentile of z-statistic for faces activation	5.88 ± 0.49	5.93 ± 1.95	99.00	-0.026	0.539	0.849
Multimodal	90th percentile of z-statistic for shapes activation	4.58 ± 0.46	4.80 ± 1.48	-0.30	-0.152	0.766	0.919
Multimodal	90th percentile of z-statistic for faces-shapes contrast	6.64 ± 1.54	6.03 ± 2.60	0.47	0.237	0.643	0.878
Multimodal	Left amygdala habituation for faces condition	-0.02 ± 0.22	-0.01 ± 0.31	119.00	-0.047	0.946	0.979
Multimodal	Right amygdala habituation for faces condition	0.06 ± 0.32	0.01 ± 0.27	0.31	0.159	0.757	0.919
Multimodal	Left amygdala habituation for shapes condition	-0.04 ± 0.15	0.03 ± 0.33	102.00	-0.207	0.595	0.866
Multimodal	Right amygdala habituation for shapes condition	-0.08 ± 0.18	0.00 ± 0.27	102.00	-0.317	0.595	0.866
Multimodal	ADHD Demontis2022	-0.21 ± 1.12	0.04 ± 1.06	-0.45	-0.232	0.651	0.881
Multimodal	ALCDEP Walters2018	-0.16 ± 0.10	0.04 ± 0.98	109.00	-0.209	0.733	0.908
Multimodal	AN Watson2019	-0.39 ± 1.63	0.14 ± 1.06	-0.93	-0.476	0.354	0.713
Multimodal	ASD Grove2019	-0.92 ± 0.81	0.04 ± 0.99	-1.88	-0.958	0.065	0.239
Multimodal	BD PGC4 2025	-0.43 ± 0.98	-0.15 ± 1.17	-0.47	-0.240	0.639	0.878
Multimodal	BMI Locke2015	0.05 ± 1.86	0.07 ± 0.88	132.50	-0.019	0.785	0.919
Multimodal	bNGF Konieczny2025	0.53 ± 0.77	-0.06 ± 1.09	1.06	0.542	0.292	0.634
Multimodal	CAD Nikpay2015	0.06 ± 1.10	-0.08 ± 1.09	0.25	0.128	0.802	0.925
Multimodal	CCL11 Konieczny2025	0.15 ± 1.02	0.18 ± 1.08	-0.05	-0.025	0.962	0.984
Multimodal	CCL2 Konieczny2025	0.14 ± 0.72	-0.12 ± 0.79	156.00	0.332	0.360	0.716
Multimodal	CCL3 Konieczny2025	0.03 ± 1.20	-0.08 ± 0.90	0.23	0.120	0.815	0.930
Multimodal	CCL4 Konieczny2025	-0.83 ± 0.74	-0.01 ± 0.88	-1.82	-0.927	0.074	0.263
Multimodal	CCL7 Konieczny2025	-0.59 ± 1.35	-0.00 ± 0.97	-1.14	-0.584	0.257	0.594
Multimodal	CRP Said2022	0.28 ± 0.43	0.01 ± 0.98	0.56	0.288	0.575	0.860
Multimodal	CSF1 Konieczny2025	-0.17 ± 0.73	0.01 ± 0.99	-0.36	-0.186	0.716	0.908
Multimodal	CSF3 Konieczny2025	-0.65 ± 0.87	-0.16 ± 0.87	-1.08	-0.550	0.285	0.624
Multimodal	CTACK Konieczny2025	-0.33 ± 1.44	-0.01 ± 1.03	-0.59	-0.300	0.559	0.859
Multimodal	CUD Johnson2020	-0.14 ± 0.51	-0.16 ± 0.98	118.50	0.025	0.935	0.976
Multimodal	CXCL1 Konieczny2025	0.86 ± 0.94	0.21 ± 0.98	1.29	0.656	0.203	0.527
Multimodal	CXCL10 Konieczny2025	-0.52 ± 1.12	0.10 ± 1.10	-1.09	-0.556	0.280	0.618
Multimodal	CXCL12 Konieczny2025	-0.14 ± 0.92	-0.01 ± 0.93	108.50	-0.135	0.723	0.908
Multimodal	CXCL9 Konieczny2025	-0.78 ± 0.69	-0.02 ± 0.91	-1.63	-0.830	0.109	0.348
Multimodal	FGFb Konieczny2025	-0.04 ± 1.29	-0.11 ± 0.79	0.16	0.079	0.877	0.951
Multimodal	GAD FinnGen2024	0.43 ± 0.44	-0.01 ± 1.03	0.84	0.430	0.402	0.760
Multimodal	HbA1c Willems2023	-0.53 ± 0.87	0.00 ± 1.15	-0.90	-0.460	0.371	0.728
Multimodal	HDL Graham2021	-0.22 ± 0.95	-0.29 ± 1.16	0.11	0.058	0.910	0.968
Multimodal	HGF Konieczny2025	0.25 ± 0.69	0.14 ± 1.13	0.19	0.094	0.854	0.947

Multimodal	IFNg Konieczny2025	-0.20 ± 0.58	-0.05 ± 1.05	-0.28	-0.143	0.779	0.919
Multimodal	IL10 Konieczny2025	-0.44 ± 1.16	-0.05 ± 0.90	-0.83	-0.426	0.407	0.760
Multimodal	IL13 Konieczny2025	0.06 ± 0.62	-0.02 ± 0.97	0.16	0.081	0.874	0.951
Multimodal	IL16 Konieczny2025	0.11 ± 0.89	-0.14 ± 1.07	0.46	0.233	0.650	0.881
Multimodal	IL17 Konieczny2025	-0.43 ± 0.36	-0.08 ± 1.08	-0.65	-0.329	0.521	0.845
Multimodal	IL18 Konieczny2025	0.56 ± 0.53	0.23 ± 0.94	143.00	0.349	0.576	0.860
Multimodal	IL1b Konieczny2025	-0.81 ± 0.71	-0.14 ± 0.94	-1.40	-0.712	0.167	0.471
Multimodal	IL1RA Konieczny2025	-0.42 ± 1.50	0.14 ± 0.90	-1.16	-0.591	0.251	0.584
Multimodal	IL2 Konieczny2025	-0.74 ± 1.23	0.03 ± 1.01	-1.46	-0.745	0.149	0.433
Multimodal	IL2RA Konieczny2025	0.11 ± 0.55	0.08 ± 1.09	0.04	0.022	0.965	0.984
Multimodal	IL4 Konieczny2025	-0.21 ± 1.13	-0.05 ± 1.05	-0.29	-0.150	0.769	0.919
Multimodal	IL5 Konieczny2025	0.09 ± 0.53	0.04 ± 1.01	0.09	0.046	0.928	0.972
Multimodal	IL6 Konieczny2025	0.84 ± 1.26	-0.06 ± 0.95	1.80	0.920	0.076	0.269
Multimodal	IL7 Konieczny2025	-0.02 ± 0.89	0.00 ± 0.94	-0.04	-0.019	0.970	0.985
Multimodal	IL8 Konieczny2025	-0.55 ± 1.22	-0.12 ± 1.02	-0.82	-0.417	0.417	0.772
Multimodal	IL9 Konieczny2025	-0.04 ± 0.53	-0.09 ± 1.06	0.09	0.048	0.925	0.972
Multimodal	LDL Graham2021	0.03 ± 0.93	-0.07 ± 1.00	0.19	0.096	0.852	0.947
Multimodal	MDD PGC4 2025	-0.77 ± 1.06	0.09 ± 0.99	-1.69	-0.861	0.096	0.322
Multimodal	MIF Konieczny2025	0.04 ± 1.10	-0.10 ± 1.01	0.26	0.134	0.794	0.919
Multimodal	NEUROT DeMoor2015	-0.01 ± 0.42	-0.01 ± 1.03	-0.01	-0.003	0.995	0.997
Multimodal	OCD PGC3 2018	-0.14 ± 0.74	0.05 ± 0.99	103.50	-0.188	0.623	0.876
Multimodal	PDGFBB Konieczny2025	0.15 ± 0.64	-0.09 ± 0.96	0.49	0.250	0.626	0.876
Multimodal	PTSD Nievergelt2024	-0.72 ± 0.97	0.04 ± 0.90	-1.62	-0.825	0.111	0.350
Multimodal	RANTES Konieczny2025	0.82 ± 0.32	0.18 ± 0.91	1.39	0.710	0.169	0.473
Multimodal	SCF Konieczny2025	-0.75 ± 0.42	0.13 ± 1.18	-1.48	-0.752	0.145	0.426
Multimodal	SCGFb Konieczny2025	-0.14 ± 0.42	-0.02 ± 1.15	-0.19	-0.098	0.848	0.947
Multimodal	SCZ Trubetskoy2022	0.08 ± 1.24	-0.26 ± 1.04	0.62	0.319	0.534	0.849
Multimodal	T2D Verma2024	0.07 ± 1.31	0.22 ± 0.98	-0.28	-0.143	0.781	0.919
Multimodal	TNFa Konieczny2025	-0.08 ± 0.67	0.10 ± 1.00	-0.34	-0.175	0.733	0.908
Multimodal	TNFb Konieczny2025	-0.12 ± 1.17	0.07 ± 1.00	-0.37	-0.188	0.714	0.908
Multimodal	TRAIL Konieczny2025	0.54 ± 0.85	-0.00 ± 1.16	0.91	0.464	0.366	0.722
Multimodal	TRIG Graham2021	0.61 ± 1.00	0.12 ± 1.02	0.95	0.483	0.347	0.702
Multimodal	VEGF Konieczny2025	1.40 ± 0.66	-0.09 ± 0.95	3.07	1.567	0.003	0.073

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; DTI, diffusion tensor imaging; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; fMRI, functional magnetic resonance imaging; GM, grey matter; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA, interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; rs-fMRI, resting-state fMRI; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; Sneg, strength of negative resting-state connections; Spos, strength of positive resting-state connections; T2D, type 2 diabetes; t-fMRI, task-based fMRI; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05

Table A18. Outcome variable comparisons between clusters resulting from the significant stratification models among the MDD sample of the OSR dataset.

Model	Variable	C10	C11	Statistic	Effect size	p-value	q-value
DTI	BMI	24.88 ± 5.01	25.13 ± 4.50	2823.00	-0.052	0.440	0.810
	Number of depressive episodes	4.77 ± 4.94	6.27 ± 6.80	2843.50	-0.251	0.330	0.810
	History of suicide attempts	0=60; 1=17	0=61; 1=19	0.06	1.099	0.803	0.994
	HAM-D – total score	21.81 ± 6.74	22.46 ± 7.23	-0.57	-0.091	0.567	0.810
	HAM-D – item 3	0=28; 1=22; 2=11; 3=5; 4=1	0=27; 1=30; 2=12; 3=7; 4=1	2434.00	0.043	0.539	0.810
	BDI – total score	16.59 ± 8.14	16.32 ± 8.29	0.18	0.033	0.860	0.994
	BDI – item 8	0=37; 1=17; 2=4	0=26; 1=16; 2=11; 3=3	1249.00	0.251	0.018	0.352
	BACS - Verbal memory	35.85 ± 11.27	35.99 ± 10.93	-0.07	-0.012	0.940	0.994
	BACS - Working Memory	17.00 ± 5.36	16.61 ± 6.75	2831.50	0.064	0.421	0.810
	BACS - Motor speed	66.46 ± 15.99	65.46 ± 20.07	0.32	0.055	0.748	0.994
	BACS - Verbal fluency	12.76 ± 5.45	11.63 ± 4.62	2787.50	0.223	0.528	0.810
	BACS - Processing speed	39.69 ± 14.21	34.89 ± 13.76	3109.50	0.341	0.038	0.352
	BACS - Executive function	14.15 ± 4.02	13.84 ± 5.11	2157.50	0.066	0.945	0.994
	Cardiovascular disorders	0=65; 1=12	0=59; 1=22	3.13	2.020	0.077	0.384
	Diabetes	0=76; 1=1	0=79; 1=2	/	1.924	1.000	1.000
	TRD – history	0=56; 1=16	0=54; 1=26	2.00	1.685	0.157	0.524
	TRD – current	0=57; 1=15	0=52; 1=28	3.75	2.046	0.053	0.352
t-fMRI	BMI	25.91 ± 5.86	24.31 ± 3.78	742.50	0.355	0.432	0.962
	Number of depressive episodes	7.04 ± 8.19	4.66 ± 4.66	872.00	0.403	0.042	0.476
	History of suicide attempts	0=19; 1=4	0=45; 1=14	0.39	1.478	0.533	0.962
	HAM-D – total score	22.09 ± 7.54	21.60 ± 6.38	0.29	0.072	0.769	0.974
	HAM-D – item 3	0=9; 1=8; 2=4; 3=1	0=23; 1=15; 2=10; 3=3	569.00	0.000	0.923	0.993
	BDI – total score	15.40 ± 7.53	17.18 ± 7.75	-0.87	-0.229	0.385	0.962
	BDI – item 8	0=10; 1=7; 2=2; 3=1	0=22; 1=18; 2=8; 3=1	463.50	0.031	0.709	0.962
	BACS - Verbal memory	36.33 ± 9.13	37.51 ± 10.71	-0.45	-0.113	0.657	0.962
	BACS - Working Memory	16.40 ± 4.22	16.71 ± 7.46	565.50	-0.046	0.953	0.993
	BACS - Motor speed	60.53 ± 14.56	63.34 ± 15.87	-0.68	-0.179	0.498	0.962
	BACS - Verbal fluency	11.48 ± 4.29	11.46 ± 5.16	0.01	0.002	0.993	0.993
	BACS - Processing speed	36.35 ± 12.17	37.71 ± 12.81	-0.41	-0.107	0.680	0.962
	BACS - Executive function	14.11 ± 4.57	13.89 ± 4.56	0.18	0.047	0.858	0.993
	Cardiovascular disorders	0=17; 1=6	0=46; 1=13	0.15	0.801	0.696	0.962
	TRD – history	0=18; 1=3	0=35; 1=21	3.84	3.600	0.050	0.476
	TRD – current	0=16; 1=5	0=39; 1=17	0.32	1.395	0.571	0.962

PGSs	BMI	24.78 ± 4.42	24.95 ± 4.83	3514.00	-0.036	0.927	1.000
	Number of depressive episodes	4.99 ± 4.27	5.51 ± 5.84	3482.00	-0.100	0.684	1.000
	History of suicide attempts	0=62; 1=21	0=72; 1=14	2.09	0.574	0.148	0.877
	HAM-D – total score	21.94 ± 6.70	22.26 ± 7.07	-0.31	-0.047	0.760	1.000
	HAM-D – item 3	0=26; 1=25; 2=13; 3=7; 4=2	0=36; 1=27; 2=11; 3=7	3300.50	-0.113	0.188	0.877
	BDI – total score	16.98 ± 8.44	15.59 ± 7.47	0.97	0.174	0.333	0.885
	BDI – item 8	0=32; 1=21; 2=5; 3=1	0=37; 1=14; 2=10; 3=2	1858.00	0.037	1.000	1.000
	BACS - Verbal memory	37.49 ± 11.27	34.61 ± 10.77	3595.50	0.260	0.095	0.877
	BACS - Working Memory	17.19 ± 5.41	16.77 ± 6.36	3401.00	0.071	0.259	0.877
	BACS - Motor speed	67.26 ± 16.68	64.80 ± 18.55	0.85	0.139	0.398	0.885
	BACS - Verbal fluency	12.56 ± 5.31	12.05 ± 4.59	3015.50	0.103	0.939	1.000
	BACS - Processing speed	38.44 ± 14.91	37.16 ± 13.54	0.56	0.089	0.576	1.000
	BACS - Executive function	14.47 ± 4.69	13.81 ± 4.55	2794.00	0.143	0.263	0.877
	Cardiovascular disorders	0=64; 1=19	0=67; 1=20	0.00	1.005	0.988	1.000
	Diabetes	0=82; 1=1	0=84; 1=3	/	2.929	0.621	1.000
	TRD – history	0=53; 1=28	0=64; 1=19	2.73	0.562	0.098	0.877
	TRD – current	0=58; 1=23	0=58; 1=25	0.06	1.087	0.808	1.000
Multimodal	BMI	24.87 ± 4.93	24.31 ± 4.25	0.25	0.128	0.803	1.000
	Number of depressive episodes	4.75 ± 3.59	4.95 ± 4.68	127.50	-0.043	0.889	1.000
	History of suicide attempts	0=4	0=47; 1=14	/	2.747	0.569	1.000
	HAM-D – total score	20.67 ± 9.07	21.44 ± 6.58	-0.20	-0.115	0.845	1.000
	HAM-D – item 3	0=1; 1=1; 2=1	0=26; 1=18; 2=11; 3=2	97.50	-0.048	0.676	1.000
	BDI – total score	19.25 ± 1.89	16.60 ± 8.10	131.00	0.332	0.399	1.000
	BDI – item 8	0=1; 1=3	0=27; 1=16; 2=8; 3=1	118.50	-0.025	0.626	1.000
	BACS - Verbal memory	42.75 ± 2.75	36.78 ± 10.68	165.50	0.565	0.185	1.000
	BACS - Working Memory	16.75 ± 3.77	16.15 ± 6.98	131.00	0.086	0.723	1.000
	BACS - Motor speed	72.50 ± 8.70	63.74 ± 15.60	1.11	0.565	0.273	1.000
	BACS - Verbal fluency	12.25 ± 1.89	11.67 ± 4.52	0.25	0.129	0.802	1.000
	BACS - Processing speed	42.50 ± 5.45	36.91 ± 13.17	0.84	0.428	0.405	1.000
	BACS - Executive function	14.50 ± 5.07	13.66 ± 4.63	0.35	0.178	0.729	1.000
	Cardiovascular disorders	0=4	0=45; 1=16	/	3.264	0.565	1.000
	TRD – history	0=3; 1=1	0=38; 1=18	/	1.421	1.000	1.000
	TRD – current	0=4	0=39; 1=17	/	3.987	0.570	1.000

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; BACS, Brief Assessment of Cognition in Schizophrenia; BD, bipolar disorder; BDI-SF, Beck Depression Inventory; BMI, body mass index; CI, cluster; HAM-D, Hamilton Depression Rating Scale; MDD, major depressive disorder; TRD, treatment-resistant depression.

Table A19. Input feature comparisons between clusters resulting from the significant stratification models among the MDD and BD sample of the OSR dataset.

Model	Variable	C10	C11	Statistic	Effect size	p-value	q-value
DTI	Mean FA in anterior corona radiata L	0.42 ± 0.03	0.44 ± 0.02	6137.50	-1.152	<0.001	<0.001*
DTI	Mean FA in anterior corona radiata R	0.42 ± 0.03	0.45 ± 0.03	7025.00	-1.023	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule L	0.55 ± 0.02	0.58 ± 0.02	5165.50	-1.283	<0.001	<0.001*
DTI	Mean FA in anterior limb of internal capsule R	0.56 ± 0.02	0.58 ± 0.02	-10.39	-1.132	<0.001	<0.001*
DTI	Mean FA in body of corpus callosum	0.65 ± 0.03	0.69 ± 0.02	4468.00	-1.451	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle L	0.67 ± 0.02	0.70 ± 0.02	-12.59	-1.372	<0.001	<0.001*
DTI	Mean FA in cerebral peduncle R	0.67 ± 0.03	0.70 ± 0.03	-11.13	-1.213	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus L	0.55 ± 0.03	0.59 ± 0.03	-11.04	-1.202	<0.001	<0.001*
DTI	Mean FA in cingulum cingulate gyrus R	0.53 ± 0.04	0.55 ± 0.03	-6.79	-0.740	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus L	0.46 ± 0.03	0.49 ± 0.03	-8.21	-0.894	<0.001	<0.001*
DTI	Mean FA in cingulum hippocampus R	0.46 ± 0.03	0.49 ± 0.03	-8.45	-0.921	<0.001	<0.001*
DTI	Mean FA in corticospinal tract L	0.52 ± 0.03	0.55 ± 0.03	-9.23	-1.005	<0.001	<0.001*
DTI	Mean FA in corticospinal tract R	0.50 ± 0.03	0.53 ± 0.03	7402.00	-0.921	<0.001	<0.001*
DTI	Mean FA in external capsule L	0.40 ± 0.02	0.43 ± 0.02	5274.00	-1.267	<0.001	<0.001*
DTI	Mean FA in external capsule R	0.40 ± 0.03	0.42 ± 0.02	-8.46	-0.922	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis L	0.52 ± 0.03	0.56 ± 0.03	-11.14	-1.214	<0.001	<0.001*
DTI	Mean FA in fornix cres+stria terminalis R	0.53 ± 0.03	0.56 ± 0.03	7357.00	-0.981	<0.001	<0.001*
DTI	Mean FA in fornix	0.44 ± 0.07	0.47 ± 0.07	11109.00	-0.405	<0.001	<0.001*
DTI	Mean FA in genu of corpus callosum	0.66 ± 0.03	0.69 ± 0.03	-10.37	-1.129	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle L	0.53 ± 0.03	0.56 ± 0.03	5643.00	-1.219	<0.001	<0.001*
DTI	Mean FA in inferior cerebellar peduncle R	0.53 ± 0.03	0.56 ± 0.02	-11.41	-1.243	<0.001	<0.001*
DTI	Mean FA in medial lemniscus L	0.56 ± 0.03	0.59 ± 0.02	6802.00	-1.057	<0.001	<0.001*
DTI	Mean FA in medial lemniscus R	0.56 ± 0.03	0.59 ± 0.02	6291.00	-1.128	<0.001	<0.001*
DTI	Mean FA in middle cerebellar peduncle	0.54 ± 0.02	0.56 ± 0.02	-9.64	-1.050	<0.001	<0.001*
DTI	Mean FA in pontine crossing tract	0.45 ± 0.03	0.48 ± 0.03	-7.57	-0.825	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata L	0.44 ± 0.02	0.47 ± 0.02	-12.64	-1.377	<0.001	<0.001*
DTI	Mean FA in posterior corona radiata R	0.45 ± 0.02	0.48 ± 0.02	4708.00	-1.382	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule L	0.65 ± 0.03	0.68 ± 0.03	5273.00	-1.245	<0.001	<0.001*
DTI	Mean FA in posterior limb of internal capsule R	0.64 ± 0.02	0.67 ± 0.03	5938.00	-1.171	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation L	0.57 ± 0.03	0.61 ± 0.03	-11.54	-1.257	<0.001	<0.001*
DTI	Mean FA in posterior thalamic radiation R	0.56 ± 0.03	0.60 ± 0.03	-10.85	-1.182	<0.001	<0.001*
DTI	Mean FA in retrolenticular part of internal capsule L	0.58 ± 0.03	0.61 ± 0.02	-10.65	-1.160	<0.001	<0.001*

DTI	Mean FA in retrolenticular part of internal capsule R	0.56 ± 0.03	0.58 ± 0.03	8847.50	-0.762	<0.001	<0.001*
DTI	Mean FA in sagittal stratum L	0.53 ± 0.03	0.57 ± 0.03	-12.51	-1.363	<0.001	<0.001*
DTI	Mean FA in sagittal stratum R	0.53 ± 0.03	0.56 ± 0.02	5707.00	-1.195	<0.001	<0.001*
DTI	Mean FA in splenium of corpus callosum	0.75 ± 0.02	0.77 ± 0.02	-11.23	-1.224	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle L	0.65 ± 0.03	0.68 ± 0.03	-11.09	-1.208	<0.001	<0.001*
DTI	Mean FA in superior cerebellar peduncle R	0.64 ± 0.03	0.68 ± 0.03	-10.69	-1.165	<0.001	<0.001*
DTI	Mean FA in superior corona radiata L	0.45 ± 0.02	0.47 ± 0.02	-12.21	-1.330	<0.001	<0.001*
DTI	Mean FA in superior corona radiata R	0.44 ± 0.02	0.47 ± 0.02	6781.00	-1.026	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus L	0.43 ± 0.04	0.46 ± 0.03	7798.00	-0.870	<0.001	<0.001*
DTI	Mean FA in superior fronto-occipital fasciculus R	0.43 ± 0.04	0.45 ± 0.04	-6.33	-0.690	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus L	0.47 ± 0.02	0.51 ± 0.02	-13.30	-1.449	<0.001	<0.001*
DTI	Mean FA in superior longitudinal fasciculus R	0.47 ± 0.02	0.49 ± 0.02	-9.55	-1.040	<0.001	<0.001*
DTI	Mean FA in tapetum L	0.55 ± 0.05	0.60 ± 0.05	-8.06	-0.878	<0.001	<0.001*
DTI	Mean FA in tapetum R	0.52 ± 0.05	0.57 ± 0.05	-9.29	-1.012	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus L	0.47 ± 0.03	0.49 ± 0.03	-6.65	-0.724	<0.001	<0.001*
DTI	Mean FA in uncinate fasciculus R	0.49 ± 0.04	0.51 ± 0.04	-6.34	-0.691	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata L	0.12 ± 0.00	0.12 ± 0.00	6.23	0.679	<0.001	<0.001*
DTI	Mean AD in anterior corona radiata R	0.12 ± 0.01	0.12 ± 0.00	5.40	0.588	<0.001	<0.001*
DTI	Mean AD in anterior limb of internal capsule L	0.13 ± 0.00	0.12 ± 0.00	17203.00	0.330	0.002	0.003*
DTI	Mean AD in anterior limb of internal capsule R	0.13 ± 0.00	0.13 ± 0.00	1.86	0.202	0.064	0.077
DTI	Mean AD in body of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	5.78	0.630	<0.001	<0.001*
DTI	Mean AD in cerebral peduncle L	0.14 ± 0.01	0.14 ± 0.01	14450.00	0.029	0.981	0.981
DTI	Mean AD in cerebral peduncle R	0.14 ± 0.01	0.14 ± 0.01	1.00	0.109	0.319	0.351
DTI	Mean AD in cingulum cingulate gyrus L	0.13 ± 0.01	0.13 ± 0.01	0.08	0.009	0.937	0.944
DTI	Mean AD in cingulum cingulate gyrus R	0.13 ± 0.01	0.13 ± 0.01	2.39	0.260	0.018	0.022*
DTI	Mean AD in cingulum hippocampus L	0.13 ± 0.01	0.13 ± 0.01	13924.50	-0.036	0.581	0.606
DTI	Mean AD in cingulum hippocampus R	0.13 ± 0.01	0.13 ± 0.01	14198.50	-0.029	0.802	0.825
DTI	Mean AD in corticospinal tract L	0.12 ± 0.01	0.12 ± 0.01	-0.71	-0.077	0.478	0.506
DTI	Mean AD in corticospinal tract R	0.12 ± 0.01	0.12 ± 0.01	0.16	0.018	0.872	0.884
DTI	Mean AD in external capsule L	0.11 ± 0.00	0.11 ± 0.00	17350.00	0.316	0.001	0.002*
DTI	Mean AD in external capsule R	0.11 ± 0.00	0.11 ± 0.00	16775.50	0.265	0.010	0.013*
DTI	Mean AD in fornix cres+stria terminalis L	0.14 ± 0.01	0.14 ± 0.01	15187.00	0.112	0.405	0.432
DTI	Mean AD in fornix cres+stria terminalis R	0.14 ± 0.01	0.14 ± 0.01	15847.00	0.195	0.119	0.137
DTI	Mean AD in fornix	0.22 ± 0.02	0.22 ± 0.02	15324.50	0.098	0.325	0.355
DTI	Mean AD in genu of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	18641.00	0.474	<0.001	<0.001*
DTI	Mean AD in inferior cerebellar peduncle L	0.12 ± 0.01	0.12 ± 0.01	-1.61	-0.176	0.108	0.125

DTI	Mean AD in inferior cerebellar peduncle R	0.12 ± 0.01	0.12 ± 0.01	-2.47	-0.269	0.014	0.018*
DTI	Mean AD in medial lemniscus L	0.13 ± 0.01	0.13 ± 0.01	-2.06	-0.224	0.040	0.049*
DTI	Mean AD in medial lemniscus R	0.13 ± 0.01	0.13 ± 0.01	13228.50	-0.165	0.188	0.212
DTI	Mean AD in middle cerebellar peduncle	0.12 ± 0.00	0.12 ± 0.00	0.39	0.043	0.693	0.718
DTI	Mean AD in pontine crossing tract	0.11 ± 0.01	0.11 ± 0.01	-0.95	-0.104	0.342	0.370
DTI	Mean AD in posterior corona radiata L	0.12 ± 0.01	0.12 ± 0.01	18108.50	0.449	<0.001	<0.001*
DTI	Mean AD in posterior corona radiata R	0.13 ± 0.01	0.13 ± 0.01	5.89	0.642	<0.001	<0.001*
DTI	Mean AD in posterior limb of internal capsule L	0.13 ± 0.01	0.13 ± 0.01	16020.00	0.185	0.080	0.096
DTI	Mean AD in posterior limb of internal capsule R	0.13 ± 0.01	0.13 ± 0.01	15567.50	0.089	0.211	0.235
DTI	Mean AD in posterior thalamic radiation L	0.15 ± 0.01	0.15 ± 0.01	15786.50	0.169	0.136	0.154
DTI	Mean AD in posterior thalamic radiation R	0.15 ± 0.01	0.15 ± 0.01	16238.50	0.174	0.047	0.057
DTI	Mean AD in retrolenticular part of internal capsule L	0.14 ± 0.01	0.14 ± 0.01	1.51	0.164	0.133	0.152
DTI	Mean AD in retrolenticular part of internal capsule R	0.14 ± 0.01	0.14 ± 0.01	3.84	0.419	<0.001	<0.001*
DTI	Mean AD in sagittal stratum L	0.14 ± 0.01	0.14 ± 0.01	2.14	0.233	0.033	0.041*
DTI	Mean AD in sagittal stratum R	0.14 ± 0.00	0.14 ± 0.01	18780.00	0.496	<0.001	<0.001*
DTI	Mean AD in splenium of corpus callosum	0.16 ± 0.01	0.16 ± 0.01	3.35	0.365	<0.001	0.001*
DTI	Mean AD in superior cerebellar peduncle L	0.16 ± 0.01	0.16 ± 0.01	14939.50	0.063	0.574	0.604
DTI	Mean AD in superior cerebellar peduncle R	0.16 ± 0.01	0.16 ± 0.01	0.92	0.100	0.358	0.385
DTI	Mean AD in superior corona radiata L	0.11 ± 0.00	0.11 ± 0.00	19071.50	0.555	<0.001	<0.001*
DTI	Mean AD in superior corona radiata R	0.11 ± 0.00	0.11 ± 0.00	19214.50	0.566	<0.001	<0.001*
DTI	Mean AD in superior fronto-occipital fasciculus L	0.11 ± 0.01	0.11 ± 0.01	15975.00	0.230	0.089	0.105
DTI	Mean AD in superior fronto-occipital fasciculus R	0.11 ± 0.01	0.11 ± 0.01	14581.00	0.047	0.867	0.884
DTI	Mean AD in superior longitudinal fasciculus L	0.12 ± 0.00	0.12 ± 0.00	4.29	0.467	<0.001	<0.001*
DTI	Mean AD in superior longitudinal fasciculus R	0.12 ± 0.00	0.12 ± 0.00	5.00	0.545	<0.001	<0.001*
DTI	Mean AD in tapetum L	0.16 ± 0.01	0.16 ± 0.01	16319.00	0.248	0.038	0.047*
DTI	Mean AD in tapetum R	0.17 ± 0.01	0.17 ± 0.01	17109.50	0.298	0.003	0.004*
DTI	Mean AD in uncinate fasciculus L	0.13 ± 0.01	0.13 ± 0.01	-1.15	-0.126	0.250	0.277
DTI	Mean AD in uncinate fasciculus R	0.13 ± 0.01	0.13 ± 0.01	-1.72	-0.187	0.087	0.102
DTI	Mean RD in anterior corona radiata L	0.06 ± 0.00	0.06 ± 0.00	13.02	1.418	<0.001	<0.001*
DTI	Mean RD in anterior corona radiata R	0.06 ± 0.00	0.06 ± 0.00	23727.50	1.323	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule L	0.05 ± 0.00	0.05 ± 0.00	24985.50	1.457	<0.001	<0.001*
DTI	Mean RD in anterior limb of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	23233.50	1.198	<0.001	<0.001*
DTI	Mean RD in body of corpus callosum	0.05 ± 0.00	0.04 ± 0.00	24989.00	1.549	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle L	0.04 ± 0.00	0.04 ± 0.00	24450.50	1.428	<0.001	<0.001*
DTI	Mean RD in cerebral peduncle R	0.04 ± 0.00	0.04 ± 0.00	11.92	1.298	<0.001	<0.001*

DTI	Mean RD in cingulum cingulate gyrus L	0.05 ± 0.00	0.05 ± 0.00	13.83	1.506	<0.001	<0.001*
DTI	Mean RD in cingulum cingulate gyrus R	0.05 ± 0.00	0.05 ± 0.00	10.75	1.171	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus L	0.06 ± 0.00	0.06 ± 0.00	6.22	0.678	<0.001	<0.001*
DTI	Mean RD in cingulum hippocampus R	0.06 ± 0.00	0.06 ± 0.00	7.94	0.865	<0.001	<0.001*
DTI	Mean RD in corticospinal tract L	0.05 ± 0.00	0.05 ± 0.00	21361.00	0.859	<0.001	<0.001*
DTI	Mean RD in corticospinal tract R	0.05 ± 0.00	0.05 ± 0.00	6.71	0.731	<0.001	<0.001*
DTI	Mean RD in external capsule L	0.06 ± 0.00	0.06 ± 0.00	23322.00	1.199	<0.001	<0.001*
DTI	Mean RD in external capsule R	0.06 ± 0.00	0.06 ± 0.00	20998.00	0.838	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis L	0.06 ± 0.01	0.05 ± 0.00	21977.50	1.006	<0.001	<0.001*
DTI	Mean RD in fornix cres+stria terminalis R	0.06 ± 0.01	0.05 ± 0.00	22190.00	1.031	<0.001	<0.001*
DTI	Mean RD in fornix	0.12 ± 0.03	0.11 ± 0.03	16550.00	0.248	0.020	0.025*
DTI	Mean RD in genu of corpus callosum	0.05 ± 0.00	0.04 ± 0.00	11.71	1.276	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle L	0.05 ± 0.00	0.05 ± 0.00	22962.00	1.139	<0.001	<0.001*
DTI	Mean RD in inferior cerebellar peduncle R	0.05 ± 0.00	0.05 ± 0.00	22613.50	1.088	<0.001	<0.001*
DTI	Mean RD in medial lemniscus L	0.05 ± 0.00	0.05 ± 0.00	20689.50	0.791	<0.001	<0.001*
DTI	Mean RD in medial lemniscus R	0.05 ± 0.00	0.04 ± 0.00	21510.00	0.896	<0.001	<0.001*
DTI	Mean RD in middle cerebellar peduncle	0.05 ± 0.00	0.05 ± 0.00	22061.00	1.016	<0.001	<0.001*
DTI	Mean RD in pontine crossing tract	0.05 ± 0.00	0.05 ± 0.00	5.85	0.637	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata L	0.06 ± 0.00	0.06 ± 0.00	24344.50	1.334	<0.001	<0.001*
DTI	Mean RD in posterior corona radiata R	0.06 ± 0.00	0.06 ± 0.00	25201.50	1.579	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule L	0.04 ± 0.00	0.04 ± 0.00	12.27	1.337	<0.001	<0.001*
DTI	Mean RD in posterior limb of internal capsule R	0.04 ± 0.00	0.04 ± 0.00	11.34	1.235	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation L	0.05 ± 0.00	0.05 ± 0.00	22413.50	1.082	<0.001	<0.001*
DTI	Mean RD in posterior thalamic radiation R	0.05 ± 0.00	0.05 ± 0.00	10.41	1.134	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule L	0.05 ± 0.00	0.05 ± 0.00	23348.50	1.203	<0.001	<0.001*
DTI	Mean RD in retrolenticular part of internal capsule R	0.05 ± 0.00	0.05 ± 0.00	10.97	1.195	<0.001	<0.001*
DTI	Mean RD in sagittal stratum L	0.06 ± 0.00	0.05 ± 0.00	12.92	1.408	<0.001	<0.001*
DTI	Mean RD in sagittal stratum R	0.06 ± 0.00	0.05 ± 0.00	12.31	1.341	<0.001	<0.001*
DTI	Mean RD in splenium of corpus callosum	0.04 ± 0.00	0.03 ± 0.00	24539.00	1.457	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle L	0.05 ± 0.00	0.04 ± 0.00	9.01	0.982	<0.001	<0.001*
DTI	Mean RD in superior cerebellar peduncle R	0.05 ± 0.00	0.04 ± 0.00	22163.00	0.977	<0.001	<0.001*
DTI	Mean RD in superior corona radiata L	0.06 ± 0.00	0.05 ± 0.00	25545.50	1.673	<0.001	<0.001*
DTI	Mean RD in superior corona radiata R	0.06 ± 0.00	0.05 ± 0.00	15.44	1.682	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus L	0.06 ± 0.00	0.05 ± 0.00	22707.50	1.021	<0.001	<0.001*
DTI	Mean RD in superior fronto-occipital fasciculus R	0.06 ± 0.00	0.05 ± 0.00	21185.00	0.826	<0.001	<0.001*

DTI	Mean RD in superior longitudinal fasciculus L	0.05 ± 0.00	0.05 ± 0.00	14.44	1.574	<0.001	<0.001*
DTI	Mean RD in superior longitudinal fasciculus R	0.06 ± 0.00	0.05 ± 0.00	24086.50	1.359	<0.001	<0.001*
DTI	Mean RD in tapetum L	0.06 ± 0.01	0.06 ± 0.01	20338.50	0.776	<0.001	<0.001*
DTI	Mean RD in tapetum R	0.07 ± 0.01	0.06 ± 0.01	21392.50	0.876	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus L	0.06 ± 0.00	0.06 ± 0.00	6.21	0.677	<0.001	<0.001*
DTI	Mean RD in uncinate fasciculus R	0.06 ± 0.00	0.05 ± 0.00	4.74	0.516	<0.001	<0.001*
t-fMRI	Median z-statistic (amygdala) for faces-shapes contrast	1.22 ± 0.60	0.40 ± 0.53	6368.50	1.454	<0.001	<0.001*
t-fMRI	Median z-statistic for faces activation	2.81 ± 0.61	1.44 ± 0.76	6973.50	1.971	<0.001	<0.001*
t-fMRI	Median z-statistic for shapes activation	2.41 ± 0.60	1.32 ± 0.72	10.57	1.603	<0.001	<0.001*
t-fMRI	Median z-statistic for faces-shapes contrast	3.90 ± 1.23	1.82 ± 1.11	6751.50	1.786	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic (amygdala) for faces-shapes contrast	2.94 ± 0.75	1.81 ± 0.65	6569.50	1.623	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces activation	7.32 ± 1.07	4.50 ± 1.43	7140.50	2.199	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for shapes activation	5.74 ± 0.93	3.79 ± 1.13	6859.50	1.851	<0.001	<0.001*
t-fMRI	90th percentile of z-statistic for faces-shapes contrast	7.62 ± 1.58	4.52 ± 1.82	11.84	1.797	<0.001	<0.001*
t-fMRI	Left amygdala habituation for faces condition	-0.01 ± 0.25	-0.09 ± 0.30	4545.00	0.279	0.015	0.019*
t-fMRI	Right amygdala habituation for faces condition	0.04 ± 0.24	-0.14 ± 0.34	5171.00	0.590	<0.001	<0.001*
t-fMRI	Left amygdala habituation for shapes condition	-0.01 ± 0.23	-0.01 ± 0.29	3838.00	0.021	0.777	0.777
t-fMRI	Right amygdala habituation for shapes condition	0.01 ± 0.24	-0.01 ± 0.27	4033.00	0.096	0.383	0.417
PGSs	ADHD Demontis2022	-0.07 ± 0.97	0.07 ± 1.02	-1.36	-0.136	0.175	0.270
PGSs	ALCDEP Walters2018	-0.06 ± 1.02	0.05 ± 0.98	-1.10	-0.110	0.273	0.399
PGSs	AN Watson2019	-0.16 ± 0.98	0.14 ± 1.00	-3.01	-0.302	0.003	0.007*
PGSs	ASD Grove2019	0.00 ± 0.99	0.00 ± 1.01	-0.03	-0.003	0.975	0.975
PGSs	BD PGC4 2025	-0.11 ± 1.00	0.10 ± 0.99	-2.10	-0.210	0.037	0.079
PGSs	BMI Locke2015	-0.04 ± 0.99	0.04 ± 1.00	-0.77	-0.077	0.440	0.582
PGSs	bNGF Konieczny2025	-0.32 ± 0.98	0.28 ± 0.93	-6.29	-0.630	<0.001	<0.001*
PGSs	CAD Nikpay2015	0.08 ± 0.97	-0.07 ± 1.02	1.42	0.142	0.157	0.247
PGSs	CCL11 Konieczny2025	-0.15 ± 1.03	0.13 ± 0.96	16156.50	-0.276	0.001	0.004*
PGSs	CCL2 Konieczny2025	-0.09 ± 0.97	0.08 ± 1.02	17656.00	-0.178	0.058	0.106
PGSs	CCL3 Konieczny2025	0.09 ± 0.96	-0.09 ± 1.03	1.80	0.180	0.072	0.128
PGSs	CCL4 Konieczny2025	0.03 ± 1.03	-0.02 ± 0.97	20521.00	0.052	0.550	0.623
PGSs	CCL7 Konieczny2025	-0.06 ± 1.00	0.06 ± 0.99	17657.50	-0.124	0.058	0.106
PGSs	CRP Said2022	-0.22 ± 0.98	0.19 ± 0.98	-4.17	-0.418	<0.001	<0.001*
PGSs	CSF1 Konieczny2025	0.03 ± 0.98	-0.03 ± 1.02	0.62	0.063	0.533	0.619
PGSs	CSF3 Konieczny2025	-0.05 ± 0.92	0.06 ± 1.06	18594.50	-0.110	0.281	0.402
PGSs	CTACK Konieczny2025	-0.48 ± 0.87	0.44 ± 0.89	8960.50	-1.042	<0.001	<0.001*
PGSs	CUD Johnson2020	-0.05 ± 1.00	0.05 ± 1.00	-0.98	-0.098	0.328	0.447
PGSs	CXCL1 Konieczny2025	-0.07 ± 1.02	0.05 ± 0.97	19042.00	-0.119	0.491	0.589
PGSs	CXCL10 Konieczny2025	-0.36 ± 0.98	0.32 ± 0.91	-7.23	-0.724	<0.001	<0.001*
PGSs	CXCL12 Konieczny2025	-0.16 ± 1.02	0.14 ± 0.96	-2.96	-0.297	0.003	0.008*

PGSs	CXCL9 Konieczny2025	-0.43 ± 0.88	0.38 ± 0.95	-8.75	-0.876	<0.001	<0.001*
PGSs	FGFb Konieczny2025	0.04 ± 1.02	-0.03 ± 0.98	0.75	0.075	0.456	0.582
PGSs	GAD FinnGen2024	-0.03 ± 1.00	0.03 ± 1.00	-0.57	-0.057	0.567	0.630
PGSs	HbA1c Willems2023	0.11 ± 1.00	-0.09 ± 0.99	2.06	0.206	0.040	0.080
PGSs	HDL Graham2021	0.00 ± 0.95	-0.00 ± 1.04	0.04	0.004	0.968	0.975
PGSs	HGF Konieczny2025	-0.20 ± 0.92	0.17 ± 1.04	15914.00	-0.370	<0.001	0.002*
PGSs	IFNg Konieczny2025	-0.60 ± 0.74	0.53 ± 0.89	6807.50	-1.363	<0.001	<0.001*
PGSs	IL10 Konieczny2025	-0.47 ± 0.89	0.42 ± 0.90	-9.89	-0.990	<0.001	<0.001*
PGSs	IL13 Konieczny2025	-0.67 ± 0.72	0.59 ± 0.83	-16.17	-1.619	<0.001	<0.001*
PGSs	IL16 Konieczny2025	-0.07 ± 1.00	0.07 ± 0.99	18999.00	-0.132	0.468	0.585
PGSs	IL17 Konieczny2025	-0.61 ± 0.78	0.55 ± 0.84	-14.33	-1.434	<0.001	<0.001*
PGSs	IL18 Konieczny2025	0.03 ± 0.99	-0.03 ± 1.00	20545.00	0.064	0.537	0.619
PGSs	IL1b Konieczny2025	-0.02 ± 1.01	0.02 ± 0.99	-0.44	-0.044	0.660	0.709
PGSs	IL1RA Konieczny2025	-0.10 ± 1.01	0.10 ± 0.98	-1.96	-0.196	0.051	0.099
PGSs	IL2 Konieczny2025	-0.28 ± 0.96	0.24 ± 0.97	-5.34	-0.534	<0.001	<0.001*
PGSs	IL2RA Konieczny2025	-0.10 ± 1.00	0.09 ± 0.99	17897.00	-0.183	0.092	0.154
PGSs	IL4 Konieczny2025	-0.67 ± 0.71	0.60 ± 0.83	4789.50	-1.629	<0.001	<0.001*
PGSs	IL5 Konieczny2025	-0.68 ± 0.79	0.61 ± 0.74	-16.87	-1.688	<0.001	<0.001*
PGSs	IL6 Konieczny2025	-0.27 ± 0.99	0.23 ± 0.94	-5.21	-0.521	<0.001	<0.001*
PGSs	IL7 Konieczny2025	-0.73 ± 0.72	0.65 ± 0.74	3258.00	-1.889	<0.001	<0.001*
PGSs	IL8 Konieczny2025	-0.55 ± 0.89	0.49 ± 0.83	-12.02	-1.204	<0.001	<0.001*
PGSs	IL9 Konieczny2025	-0.44 ± 0.88	0.39 ± 0.94	-9.07	-0.908	<0.001	<0.001*
PGSs	LDL Graham2021	0.06 ± 1.03	-0.05 ± 0.97	1.03	0.103	0.304	0.424
PGSs	MDD PGC4 2025	-0.11 ± 1.01	0.11 ± 0.97	-2.14	-0.215	0.033	0.073
PGSs	MIF Konieczny2025	-0.15 ± 0.95	0.13 ± 1.03	-2.83	-0.283	0.005	0.011*
PGSs	NEUROT DeMoor2015	0.02 ± 0.98	-0.01 ± 1.01	0.29	0.029	0.773	0.800
PGSs	OCD PGC3 2018	-0.05 ± 1.06	0.05 ± 0.94	18496.50	-0.091	0.245	0.367
PGSs	PDGFBB Konieczny2025	-0.25 ± 0.96	0.22 ± 0.98	-4.82	-0.482	<0.001	<0.001*
PGSs	PTSD Nievergelt2024	-0.09 ± 1.03	0.09 ± 0.95	-1.75	-0.175	0.082	0.140
PGSs	RANTES Konieczny2025	-0.25 ± 1.05	0.22 ± 0.90	14823.00	-0.478	<0.001	<0.001*
PGSs	SCF Konieczny2025	0.02 ± 1.03	-0.02 ± 0.97	0.36	0.036	0.717	0.754
PGSs	SCGFb Konieczny2025	-0.28 ± 1.03	0.24 ± 0.90	14067.00	-0.540	<0.001	<0.001*
PGSs	SCZ Trubetskoy2022	-0.04 ± 1.01	0.03 ± 1.00	-0.75	-0.075	0.455	0.582
PGSs	T2D Verma2024	-0.02 ± 1.00	0.03 ± 1.00	19018.00	-0.053	0.478	0.586
PGSs	TNFa Konieczny2025	-0.66 ± 0.80	0.59 ± 0.76	-16.06	-1.607	<0.001	<0.001*
PGSs	TNFB Konieczny2025	-0.72 ± 0.78	0.64 ± 0.69	-18.62	-1.864	<0.001	<0.001*
PGSs	TRAIL Konieczny2025	-0.11 ± 0.95	0.09 ± 1.03	-2.08	-0.208	0.038	0.080
PGSs	TRIG Graham2021	0.05 ± 0.97	-0.04 ± 1.03	20338.00	0.086	0.661	0.709
PGSs	VEGF Konieczny2025	-0.09 ± 0.99	0.07 ± 1.00	-1.64	-0.164	0.103	0.166

Abbreviations: AD, axial diffusivity; ADHD, attention and hyperactivity disorder; ALCDEP, alcohol dependence; AN, anorexia nervosa; ASD, autism spectrum disorder; BD, bipolar disorder; BMI, body mass index; bNGF, beta nerve growth factor; CAD, coronary artery disease; CCL, C-C motif ligand; Cl, cluster; CRP, C-reactive protein; CSF, colony-stimulating factor; CTACK, cutaneous T-cell attracting chemokine; CUD, cannabis use disorder; CXCL, C motif chemokine ligand; dMDD, depressed individuals with lifetime major depressive disorder; DTI, diffusion tensor imaging; FA, fractional anisotropy; FGFb, basic fibroblast growth factor; fMRI, functional magnetic resonance imaging; GM, grey matter; HDL, high-density lipoprotein; HGF, hepatocyte growth factor; ICA, independent component analysis; IFNg, interferon-gamma; IL, interleukin; IL1RA, interleukin-1 receptor antagonist; IL2RA,

*interleukin-2 receptor, alpha subunit; L, left; LDL, low-density lipoprotein; MDD, major depressive disorder; MIF, macrophage migration inhibitory factor; NEUROT, neuroticism; OCD, obsessive-compulsive disorder; PDGFbb, platelet derived growth factor BB; PGC, Psychiatric Genomics Consortium; PGS, polygenic risk score; PTSD, post-traumatic stress disorder; R, right; RANTES, regulated on activation, normal T-cell expressed and secreted; RD, radial diffusivity; rs-fMRI, resting-state fMRI; SCF, stem cell factor; SCGFb, stem cell growth factor beta; SCZ, schizophrenia; T2D, type 2 diabetes; t-fMRI, task-based fMRI; TNF, tumor necrosis factor; TRAIL, TNF-related apoptosis inducing ligand; VEGF, vascular endothelial growth factor. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05*

Table A20. Outcome variable comparisons between clusters resulting from the significant stratification models among the MDD and BD sample of the OSR dataset.

Model	Variable	C10	C11	Statistic	Effect size	p-value	q-value
DTI	BMI	26.15 ± 4.58	25.14 ± 4.82	16116.50	0.212	0.015	0.288
	Number of depressive episodes	7.23 ± 7.03	6.48 ± 6.66	14757.50	0.110	0.448	0.696
	History of suicide attempts	0=107; 1=33	0=163; 1=36	1.52	0.716	0.217	0.611
	HAM-D – total score	22.53 ± 6.14	21.59 ± 6.02	1.39	0.155	0.166	0.582
	HAM-D – item 3	0=48; 1=58; 2=18; 3=10; 4=1	0=77; 1=76; 2=20; 3=6; 4=1	13391.50	-0.103	0.094	0.395
	BDI – total score	15.79 ± 8.51	15.63 ± 7.90	7758.50	0.020	0.920	0.957
	BDI – item 8	0=54; 1=29; 2=13; 3=3	0=98; 1=37; 2=10; 3=5	8287.00	-0.103	0.074	0.390
	BACS - Verbal memory	34.77 ± 10.63	36.00 ± 11.19	-0.94	-0.112	0.349	0.611
	BACS - Working Memory	16.52 ± 5.57	17.24 ± 5.78	9066.50	-0.127	0.281	0.611
	BACS - Motor speed	65.67 ± 20.96	67.65 ± 19.10	7759.50	-0.099	0.464	0.696
	BACS - Verbal fluency	10.98 ± 4.42	11.84 ± 5.15	9274.50	-0.176	0.311	0.611
	BACS - Processing speed	34.53 ± 13.73	38.29 ± 13.50	7481.50	-0.276	0.027	0.288
	BACS - Executive function	14.54 ± 4.78	14.12 ± 4.13	6382.50	0.095	0.330	0.611
	Cardiovascular disorders	0=108; 1=36	0=165; 1=34	3.22	0.618	0.073	0.390
	Diabetes	0=136; 1=9	0=192; 1=7	1.37	0.551	0.242	0.611
	TRD – history	0=116; 1=26	0=154; 1=39	0.19	1.130	0.664	0.843
	TRD – current	0=114; 1=28	0=152; 1=41	0.12	1.098	0.733	0.855
t-fMRI	BMI	24.62 ± 3.84	26.14 ± 5.43	2945.50	-0.315	0.067	0.544
	Number of depressive episodes	5.78 ± 5.93	7.15 ± 7.28	3161.50	-0.203	0.145	0.544
	History of suicide attempts	0=65; 1=13	0=68; 1=27	3.33	1.985	0.068	0.544
	HAM-D – total score	21.17 ± 6.17	21.86 ± 6.56	2972.50	-0.106	0.646	0.822
	HAM-D – item 3	0=32; 1=22; 2=9; 3=3	0=32; 1=36; 2=15; 3=3	2545.00	0.076	0.243	0.544
	BDI – total score	16.75 ± 7.89	15.71 ± 8.79	0.74	0.124	0.463	0.749
	BDI – item 8	0=34; 1=22; 2=10; 3=3	0=41; 1=19; 2=5; 3=3	2632.50	-0.107	0.171	0.544
	BACS - Verbal memory	37.93 ± 10.19	35.52 ± 10.51	1.41	0.232	0.161	0.544
	BACS - Working Memory	17.62 ± 6.85	16.16 ± 5.36	2752.00	0.236	0.269	0.544
	BACS - Motor speed	64.03 ± 16.91	60.84 ± 19.79	1.02	0.172	0.311	0.544
	BACS - Verbal fluency	11.71 ± 4.79	10.74 ± 4.55	1.24	0.206	0.217	0.544
	BACS - Processing speed	38.42 ± 11.06	35.47 ± 14.17	1.38	0.231	0.169	0.544
	BACS - Executive function	14.12 ± 4.04	14.54 ± 4.69	2087.00	-0.096	0.580	0.819
	Cardiovascular disorders	0=63; 1=15	0=78; 1=17	0.05	0.915	0.822	0.822
	Diabetes	0=74; 1=4	0=93; 1=3	/	0.597	0.702	0.822
	TRD – history	0=55; 1=20	0=75; 1=17	1.61	0.623	0.205	0.544
	TRD – current	0=56; 1=19	0=67; 1=25	0.07	1.100	0.788	0.822
PGSs	BMI	25.44 ± 4.57	25.73 ± 4.93	18648.00	-0.061	0.785	0.928
	Number of depressive episodes	6.59 ± 6.39	6.98 ± 7.03	18599.00	-0.057	0.360	0.928
	History of suicide attempts	0=149; 1=38	0=168; 1=38	0.22	0.887	0.638	0.928
	HAM-D – total score	21.84 ± 6.00	22.27 ± 6.34	-0.67	-0.069	0.501	0.928

HAM-D – item 3	0=64; 1=74; 2=20; 3=9; 4=2	0=87; 1=79; 2=21; 3=11	17803.50	-0.059	0.253	0.928
BDI – total score	15.81 ± 8.48	16.19 ± 7.90	-0.38	-0.045	0.702	0.928
BDI – item 8	0=78; 1=43; 2=7; 3=6	0=94; 1=30; 2=17; 3=5	10141.50	-0.011	0.540	0.928
BACS - Verbal memory	37.20 ± 10.76	34.06 ± 10.93	2.61	0.289	0.010	0.202
BACS - Working Memory	16.96 ± 5.17	16.90 ± 5.93	13074.50	0.010	0.812	0.928
BACS - Motor speed	68.07 ± 17.85	65.27 ± 20.37	11606.00	0.145	0.372	0.928
BACS - Verbal fluency	11.93 ± 4.91	11.24 ± 4.58	13469.00	0.146	0.584	0.928
BACS - Processing speed	37.40 ± 13.88	35.98 ± 13.55	0.91	0.103	0.362	0.928
BACS - Executive function	14.46 ± 4.42	14.37 ± 4.33	8226.00	0.022	0.840	0.928
Cardiovascular disorders	0=151; 1=37	0=168; 1=42	0.01	1.020	0.936	0.948
Diabetes	0=179; 1=9	0=199; 1=12	0.16	1.199	0.688	0.928
TRD – history	0=147; 1=38	0=166; 1=39	0.14	0.909	0.707	0.928
TRD – current	0=144; 1=41	0=159; 1=46	0.00	1.016	0.948	0.948

Results are reported in terms of mean ± standard deviation for continuous variables and class counts for categorical variables. Abbreviations: BMI, body mass index; BACS, Brief Assessment of Cognition in Schizophrenia; BD, bipolar disorder; BDI-SF, Beck Depression Inventory; BMI, body mass index; Cl, cluster; HAM-D, Hamilton Depression Rating Scale; MDD, major depressive disorder; TRD, treatment-resistant depression.

Table A21. Outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD sample of the OSR dataset.

Model	Variable	Cluster	AUC	BA (%)	Sensitivity (%)	Specificity (%)	p-value	q-value
DTI	Cardiovascular disorders	C10	0.772	76.28	83.33	69.23	0.001	0.008*
	Cardiovascular disorders	C11	0.498	50.15	54.55	45.76	0.493	0.788
	TRD – history	C10	0.396	45.54	50.00	41.07	0.730	0.835
	TRD – history	C11	0.610	58.62	65.38	51.85	0.114	0.421
	TRD – current	C10	0.387	39.47	33.33	45.61	0.885	0.885
	TRD – current	C11	0.602	56.87	71.43	42.31	0.158	0.421
	History of suicide attempts	C10	0.479	47.25	41.18	53.33	0.620	0.827
	History of suicide attempts	C11	0.523	51.25	63.16	39.34	0.435	0.788
t-fMRI	Cardiovascular disorders	C10	0.422	42.65	50.00	35.29	0.774	0.774
	Cardiovascular disorders	C11	0.630	59.62	69.23	50.00	0.157	0.322
	TRD – current	C11	0.667	58.90	58.82	58.97	0.161	0.322
	History of suicide attempts	C11	0.452	44.76	42.86	46.67	0.725	0.774
PGSs	Cardiovascular disorders	C10	0.483	49.75	52.63	46.88	0.504	0.807
	Cardiovascular disorders	C11	0.434	43.13	40.00	46.27	0.817	0.817
	TRD – history	C10	0.457	47.94	39.29	56.60	0.602	0.807
	TRD – history	C11	0.568	52.38	57.89	46.88	0.381	0.807
	TRD – current	C10	0.549	54.12	56.52	51.72	0.307	0.807
	TRD – current	C11	0.494	48.72	44.00	53.45	0.563	0.807
	TRD	C10	0.531	58.33	50.00	66.67	0.125	0.624
	TRD	C11	0.411	45.69	41.38	50.00	0.720	0.807
	History of suicide attempts	C10	0.673	59.98	61.90	58.06	0.080	0.624
	History of suicide attempts	C11	0.514	45.04	42.86	47.22	0.726	0.807
Multimodal	Cardiovascular disorders	C11	0.546	56.60	68.75	44.44	0.237	0.411
	History of suicide attempts	C11	0.471	51.60	50.00	53.19	0.411	0.411

*N.B. Missing models were not computed due to insufficient cases in the corresponding cluster. Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; Cl, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; PGSs, polygenic scores; t-fMRI, task-based fMRI; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05*

Table A22. Outcome variables' predictions within each cluster resulting from the significant stratification models among the MDD and BD sample of the OSR dataset.

Model	Variable	Cluster	AUC	BA	Sensitivity	Specificity	p-value	q-value
DTI	Cardiovascular disorders	CI0	0.382	43.98	44.44	43.52	0.856	0.951
	Cardiovascular disorders	CI1	0.552	52.53	52.94	52.12	0.325	0.541
	Diabetes	CI0	0.437	55.76	66.67	44.85	0.318	0.541
	Diabetes	CI1	0.542	55.65	57.14	54.17	0.304	0.541
	TRD – history	CI0	0.523	49.17	42.31	56.03	0.534	0.764
	TRD – history	CI1	0.431	40.98	38.46	43.51	0.957	0.957
	TRD – current	CI0	0.579	58.02	64.29	51.75	0.094	0.541
	TRD – current	CI1	0.524	52.62	58.54	46.71	0.325	0.541
	History of suicide attempts	CI0	0.550	55.54	60.61	50.47	0.188	0.541
	History of suicide attempts	CI1	0.491	45.21	38.89	51.53	0.805	0.951
t-fMRI	Cardiovascular disorders	CI0	0.621	64.29	66.67	61.90	0.052	0.208
	Cardiovascular disorders	CI1	0.427	46.61	47.06	46.15	0.684	0.782
	TRD – history	CI0	0.463	42.73	40.00	45.45	0.831	0.831
	TRD – history	CI1	0.574	58.90	76.47	41.33	0.130	0.346
	TRD – current	CI0	0.550	46.90	47.37	46.43	0.644	0.782
	TRD – current	CI1	0.648	61.61	68.00	55.22	0.042	0.208
	History of suicide attempts	CI0	0.450	48.46	53.85	43.08	0.553	0.782
	History of suicide attempts	CI1	0.536	55.34	51.85	58.82	0.237	0.474
PGSs	Cardiovascular disorders	CI0	0.607	57.21	59.46	54.97	0.112	0.519
	Cardiovascular disorders	CI1	0.432	41.07	35.71	46.43	0.961	0.961
	Diabetes	CI0	0.600	47.36	44.44	50.28	0.603	0.929
	Diabetes	CI1	0.804	79.90	100.00	59.80	0.001	0.010*
	TRD – history	CI0	0.511	54.84	55.26	54.42	0.208	0.519
	TRD – history	CI1	0.471	46.72	41.03	52.41	0.753	0.942
	TRD – current	CI0	0.498	48.17	46.34	50.00	0.650	0.929
	TRD – current	CI1	0.491	48.61	45.65	51.57	0.603	0.929
	History of suicide attempts	CI0	0.511	55.77	60.53	51.01	0.158	0.519
	History of suicide attempts	CI1	0.390	42.70	34.21	51.19	0.922	0.961

N.B. Missing models were not computed due to insufficient cases in the corresponding cluster. Abbreviations: AUC, area under the receiver operator curve; BA, balanced accuracy; CI, cluster; DTI, diffusion tensor imaging; fMRI, functional magnetic resonance imaging; PGSs, polygenic scores; t-fMRI, task-based fMRI; TRD, treatment-resistant depression. *Statistical significance at FDR-corrected p-value (i.e., q-value) <0.05