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Subcortical volume and white matter integrity abnormalities in major depressive disorder: findings from UK Biobank (N=4446)

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Abstract:

Background: Previous reports of altered grey and white matter structure in Major Depressive Disorder (MDD) have been inconsistent. Recent meta-analyses have, however, reported reduced hippocampal grey matter volume in MDD and reduced white matter integrity in several brain regions. The use of different diagnostic criteria, different scanners and imaging sequences may, however, obscure further anatomical differences.

Methods: In this study, we tested for differences in subcortical grey matter volume and white matter integrity between depressed individuals and controls in a large sample of subjects from the first data release of the UK Biobank imaging study of 4446 individuals, which used consistent diagnostic criteria at a single assessment centre, with a single MRI scanner and protocol.

Results: Whilst we found no significant differences in subcortical volumes, we report significant reductions in depressed individuals versus controls in global white matter integrity, as measured by fractional anisotropy (FA) (β = -0.187, p = 0.017). We also report reductions in FA in association/commissural fibres (β = -0.184, p = 0.019) and thalamic radiations (β = -0.175, p = 0.027). Examining tracts individually, we report tract-specific FA reductions in the left superior longitudinal fasciculus (β = -0.218, $p_{corrected}$ = 0.012) and superior thalamic radiation (β = -0.258, $p_{corrected}$ = 0.010) in subjects with depression.

Conclusions: Our findings highlight the need for further large adequately-powered studies of depression and provide further evidence for disrupted white matter integrity in the disorder. Future studies would focus on exploring the typical neuro-phenotype in homogenous subgroups of depression.

Introduction

Major Depression Disorder (MDD) is a common psychiatric illness, affecting between 5 and 30% of the population (1) and accounts for around 10% of all days lived with disability (2). There is therefore an urgent need to identify the mechanisms underlying MDD (3; 4) and human *in vivo* MRI has been widely applied in this search.

Many brain imaging studies have measured grey matter volume differences between healthy individuals and, predominantly clinically ascertained, individuals with MDD. On the basis that prefrontal cortex and limbic areas are fundamental to emotion processing and mood regulation (5–7), these areas have been consistently implicated in the disorder (8–11). As the use of automated methods such as voxel-based morphometry (12; 13) and Freesurfer (14; 15) have increased, this has expanded the search across the whole brain. In general, structural abnormalities have been reported across diverse brain networks in MDD. Regions including the thalamus (16), amygdala (9; 17), insula (12), caudate (14), anterior cingulate cortex (9), along with prefrontal areas like orbital prefrontal cortex (OFC)(18) and dorsal lateral prefrontal cortex (PFC)(19; 20) have been reported to be smaller in MDD versus healthy controls. However, other studies have found opposite results, showing that the volumes of such regions in patient population are comparatively larger (14; 21), or have reported null findings. This

inconsistency has been suggested to originate from the effect of limited sample sizes and other sources of heterogeneity such as sample characteristics, recruitment criteria, data acquisition and image processing (8; 22).

The lack of a single lesion or anatomically circumscribed abnormality in MDD has led many to suggest that the disorder might be due to abnormalities of brain networks affecting connections between several regions. In support of this, findings from individual studies of white matter structure in MDD have shown patterns of alteration using diffusion tensor imaging (DTI). Proxy measures of white matter integrity, including fractional anisotropy (FA) and mean diffusivity (MD), have generally been used to infer connectivity differences between groups. Decreased FA indicates lower directionality of water molecule diffusion along fibre pathways and is therefore a proxy of decreased tract integrity, whilst increased MD indicates less constrained water molecule diffusion and therefore also lower integrity.

White matter integrity of frontal-limbic tracts have been suggested to underlie clinical features in MDD due to a lack of frontal cortical control over brain regions that involve in emotion processing (23–27). Studies have reported altered water diffusivity of white matter tracts in MDD compared to healthy controls, but the implicated tracts are often inconsistent. Pérez-Iglesias *et al.* (2010) tested 31 MDD patients and 30 healthy controls,

and reported decreased FA in MDD patients in connections between prefrontal and limbic areas (e.g. fronto-occipital fasciculus, superior longitudinal fasciculus) (28). While some studies using similar sample sizes also found consistent results (29), other groups reported FA deficits in limbic areas alone (e.g. posterior thalamic radiation, posterior corona radiata) (24). Similar to the studies of subcortical volumes described above, DTI investigations of MDD have often involved small sample sizes (29; 30), with a similar risks of false positive findings.

Meta-analytic methods may help to overcome issues related to small sample sizes and are also able to formally test for between-study heterogeneity (29–31). A recent large-scale meta-analysis of subcortical structures by Schmaal *et al.* (32) tested over 1650 MDD patients and around 7000 healthy controls across 15 studies, and reported hippocampal grey matter volume reductions in MDD. No other case-control differences were found (32). Meta-analyses of white matter integrity measures in MDD have also reported FA reductions in superior longitudinal fasciculus, fronto-occipital fasciculus, and thalamic radiations (29; 30). These studies, however, often require the combination of imaging data from different scanners, using different ascertainment criteria and methodology, different clinical instruments and have differing levels of phenotypic data to pursue further research questions. Meta-analytic findings therefore highlight the pressing need to measure brain structural abnormalities in MDD using larger single-scanner

samples where robust conclusions can be made in the absence of differing study methodologies.

In the current study, we examined the volumetric structural imaging data of subcortical brain structures and tract-specific white matter integrity measures from the UK Biobank imaging study (33). UK Biobank is a study of 500,000 subjects recruited from across the United Kingdom. The dataset used in the current study is the first release of imaging data on 4446 participants who completed the brain imaging assessment. The scanning protocol was devised by UK Biobank, with consistent, compatible setting of scanner parameters and participant-friendly experimental procedures. This data therefore allowed us to explore structural changes associated with depression in a single large population-based sample using data from an individual study source with unified depression classification, and with scanning sequences and image processing procedures applied consistently across all subjects, all of whom were imaged on a single MRI scanner.

Method

Participants

In the first release of imaging data from UK Biobank, 4446 people completed the subcortical brain structural MRI measurements. The study has been approved by the National Health Service (NHS) Research Ethics Service (approval letter dated 17th June 2011, reference: 11/NW/0382), and by the UKB Access Committee (Project #4844). Written informed-consent was obtained from each subject.

Individuals from the initial pilot phase of imaging using different acquisition parameters were excluded from the current study as were, those that did not complete pre-processing quality checks (conducted by UK Biobank). In addition, scans from individuals that were identified by our internal quality check as having a structural measure that lay more than three standard deviations from the sample mean were excluded. Any participants that had a diagnosis of Parkinson's Disease, bipolar disorder, multiple personality disorder, schizophrenia, autism or intellectual disability were also excluded from the current analysis (ICD-10/9 or self-report). This resulted in data from 4165 participants with T1-weighted subcortical volumes and 3461 participants with DTI measures. Mean ages were 55.54 +/- 7.56 years for those with T1-weighted, grey matter data and 55.53 +/- 7.50 years for those with DTI, white matter integrity. The proportions of male participants are were similar in both datasets (45.83% for those providing T1-weighted data and

47.82% for those with DTI measures). Details of data exclusions were in the supplementary materials (Method, Participants).

MDD definitions

The definition of MDD used in the current study was generated based on the putative MDD category summarized previously by Smith *et al.*, as presented in supplementary materials (Table S1) (34). They generated the criteria of single episode major depression, recurrent major depression (moderate), recurrent major depression (severe) and those who were absent of depression. This category was benchmarked by testing its prevalence in the sample, and by testing for association with a number of traits, such as neuroticism (35) that have previously been associated with MDD (36). However, since the category is based on hospital admission data and depressive symptoms, which were both self-reported, rather than more formal ICD/SCID criteria, we considered the cases more strictly as 'probable' MDD and results should be viewed accordingly.

We generated two definitions of probable MDD. One was the principal MDD definition that compared MDD patients with healthy controls, while the other was the recurrent MDD definition which compared recurrent MDD patients with non-recurrent and non-MDD individuals.

The principal MDD definition included those who were categorised in single episode major depression, recurrent major depression (moderate) and

recurrent major depression (severe) as cases. The corresponding control group contained participants that were absent of depression according to the putative MDD category described by Smith *et al* (34). For the recurrent MDD definition, the case group only included recurrent major depression (both moderate and severe). The corresponding control group therefore referred to the participants without recurrent MDD, which included single episode major depression, those who were absent of depression and those who reported depressive symptoms but not enough to be specified as MDD. For the participants with any of the questions that we used for classification unanswered, they would neither be included as cases nor controls.

For each definition of probable MDD, the participants with subcortical volume data consisted of 245 MDD + 576 controls and 178 MDD + 845 controls respectively for principal and recurrent definitions. Participants with DTI data consisted of 233 MDD + 542 controls and 166 MDD + 791 controls for principal and recurrent definitions respectively.

The descriptions and demographic characteristics of each MDD definition are shown in supplementary materials (Table S1, S2). For the purposes of the current analysis, we used the principal definition of depression as the main definition as it most closely resembles the general application of typical clinical criteria. We also report results of the recurrent definition of MDD in

order to highlight differences associated with a more severe recurrent MDD diagnosis. (Supplementary materials, Table S2).

MRI acquisition and analyses

We used the imaging-derived phenotypes (IDPs) generated by UK Biobank (https://ww5.aievolution.com/hbm1601/index.cfm?do=abs.viewAbs&abs=3664). The MRI acquisition and analyses were both conducted by UK Biobank using standard protocols (http://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=2367, http://biobank.ctsu.ox.ac.uk/crystal/refer.cgi?id=1977). MRI data were acquired using a Siemens Skyra 3T scanner (https://www.healthcare.siemens.com/magnetic-resonance-imaging). The sequence for the T1-weighted data was a standard 3D MPRAGE scan (resolution 1 mm^3 isotropic voxels), while for the DTI data, the diffusion preparation was a standard ("monopolar") Stejskal-Tanner pulse sequence with a multi-shell acquisition (b = 0, 1000 and 2000 s/mm^2; resolution 8 mm^3 isotropic voxels). Images were preprocessed and analysed with the FMRIB Software Library (FSL) (http://www.fmrib.ox.ac.uk/fsl). Descriptions with detail were reported in supplementary materials (Method, MRI acquisition and preprocessing).

Segmentation of subcortical volumes was performed with FIRST (FMRIB's Integrated Registration and Segmentation Tool) (37). The volumes

of whole brain, thalamus, putamen, pallidum, hippocampus, caudate, brain stem, amygdala and accumbens were calculated for further analysis. DTI tracts were defined with AutoPtx (38) . This tractography tool maps 27 major tracts (12 bilateral tracts in both hemispheres and 3 tracts that pass across brain). Tracts were classed into three categories based on the atlas summarized by Wakana *et al.* (2004) (39) and Cox *et al.* (2016) (40): (a) *association and commissural fibres*: forceps major and minor, inferior fronto-occipital fasciculus, uncinate fasciculus, cingulum bundle and superior longitudinal fasciculus; (b) *thalamic radiations*: anterior, superior and posterior thalamic radiations; (c) *projection fibres*: corticospinal tract, acoustic radiation, medial lemniscus, middle cerebellar peduncle. The overall list of white matter tracts are listed in the supplementary materials (Table S4). Tract-averaged FA for each tract was calculated for further analysis.

Scans with severe and obvious normalization problems were excluded by UK Biobank. We also excluded outliers from analysis, as detailed above. Observations that were more than 3 standard deviation from the sample mean were classed as outliers and were excluded from the analysis of subcortical volumes. For DTI measures, participants with at least one tract-averaged FA more than 3 standard deviation from the mean for the sample were excluded for that measure. Descriptions of the sample were reported in supplementary materials (Table S2).

Statistical methods

Subcortical volumes: First, differences in global intracranial volume (ICV) associated with a probable MDD diagnosis were examined by modelling ICV as dependent variable, controlling for age, age^2 and sex. ICV was measured by adding up volumes of white matter (WM), grey matter (GM) and cerebrospinal fluid (CSF). For bilateral subcortical volumes, age, age^2, sex, hemisphere and ICV were set as covariates in a repeated-effect linear model to test the predictive effect of probable MDD definition on subcortical volumes controlling for whole brain size (lme function in nlme package of R (41)). For unilateral structures, a random-effect general linear model was applied as above, without controlling for hemisphere. We also examined the interaction of hemisphere and MDD definitions on bilateral structures. Where there showed significant effect, separate analyses on both hemispheres were conducted using the model applied on unilateral structures. All subcortical volumes were rescaled into zero mean and unitary standard deviation in order that effect sizes represent standardized scores. False Discovery Rate (FDR) multiple comparison correction was applied for tests of the 8 subcortical volumes, conducted separately for the two probable MDD definitions (Fig. 1, Table S3).

White matter integrity: In order to test for an association between probable MDD and FA, as above we used a general linear model with age, age^2 and sex as covariates and the definition of MDD as a fixed factor. First we

examined for the effects of diagnosis on global whole brain white matter integrity. The brain's white matter tracts have been shown to share a considerable proportion of variance in their microstructural properties in this (40) and other samples (42; 43). Global white matter integrity was determined using standardised approaches (44) by applying principal component analysis (PCA) on the 27 tracts to extract a latent measure. Scores of the first unrotated component of FA were extracted and set as the dependent variable of the general linear model to test the effect of probable MDD diagnosis (variance explained = 35.6%, loadings of tracts on the first latent component > 0.22). Then we separately examined three subsets of white matter tracts: (a) association and commissural fibres which include tracts connecting cortex to cortex, (b) projection fibres which consist of tracts connecting cortex to spinal cord and cortex to limbic pathways and (c) thalamic radiations including tracts that connect thalamus with cortical areas, see Cox *et al* (40). Scores of the principal unrotated component for each subset was extracted (variance explained = 43.9%, 59.3% and 37.8%; and the smallest loading on the first component = 0.34, 0.73 and 0.44 respectively for each subset) for further general linear modelling as with the global latent measure. Finally we examined the effects of depression on each tract individually. Repeated-effect linear models were used for the measures of bilateral white matter tracts correcting for hemisphere as above, while random-effect general linear models were used for the unilateral midline tracts. Both the main effect of

MDD definition and its interaction with hemisphere were tested. Where the interaction was significant, tests were applied individually for left and right sides separately. FDR correction was individually applied over the three subsets of white matter tracts as well as individual tracts (45).

Results

The effect of MDD definitions on subcortical volumes

We found no significant group effect for ICV based on the principal definition of MDD (β = 0.026, p = 0.677). There were also no significant differences between groups based on the principal definition of MDD for any of the subcortical brain regions, including the hippocampus (βs = -0.060~0.071, $p_{corrected}$ > 0.566); see Fig. 1, Table S3. No region demonstrated significant interaction of hemisphere, therefore no region was examined separately on different hemispheres.

The same models were also applied to compare groups according to the recurrent definition, see above. No subcortical regions reached significance in this definition of recurrent cases versus controls, with the greatest effect size observed for the putamen (β = 0.071, $p_{uncorrected}$ = 0.197).

The effect of probable MDD on measures of white matter integrity

Firstly we tested the effect of probable MDD on general white matter FA (gFA). For both the principal and recurrent definitions, gFA was lower in cases versus controls (β = -0.186, p = 0.016; β = -0.182, p = 0.027 respectively).

We then examined tracts categorised into association fibres, thalamic

radiations and projection fibres. We found effects of probable MDD on measures of FA in two of the three groups of tracts. Probable MDD at principal and recurrent definitions showed smaller FA values in association and commissural fibres ($\beta_{principal}$ = -0.184, $p_{principal}$ = 0.019; $\beta_{recurrent}$ = -0.187, $p_{recurrent}$ = 0.026) and in the thalamic radiations ($\beta_{principal}$ = -0.177, $p_{principal}$ = 0.024; $\beta_{recurrent}$ = -0.181, $p_{recurrent}$ = 0.031). The above p values all passed FDR correction over the three categories. No effect was found for projection fibres ($\beta_{principal}$ = -0.093, $p_{principal}$ = 0.228; $\beta_{recurrent}$ = -0.013, $p_{recurrent}$ = 0.879).

We then proceeded to compare FA values in the individual tracts between cases and controls. Initially, we tested the tracts controlling for hemisphere effects. Then we tested the interaction of hemisphere and probable MDD definitions on bilateral tracts to identify any lateralised effects. There was a significant interaction of hemisphere in superior longitudinal fasciculus for recurrent definition of probable MDD (β = 0.154, $p_{corrected}$ = 0.013). The left and right superior longitudinal fasciculi were therefore tested separately.

We found reduced FA in the superior thalamic radiations for the principal definition of MDD versus controls (β = -0.258, $p_{corrected}$ = 0.01) (Fig. 2, Table S3). There was, however, no significant effect of the recurrent MDD definition on superior thalamic radiation FA (β= -0.234, $p_{corrected}$ = 0.081) although the effect size was similar in magnitude. We also found a significant association of MDD with the left superior longitudinal fasciculus for both principal (β =

-0.218, $p_{corrected}$ = 0.043) and recurrent definitions (β = -0.269, $p_{corrected}$ =0.002). No significant association was found with right superior longitudinal fasciculus ($\beta_{principal}$ = -0.070, $p_{principal}$ = 0.437; $\beta_{recurrent}$ = -0.084, $p_{recurrent}$ = 0.407).

Discussion

In the current study we sought to determine whether MDD was associated with differences in subcortical grey matter volume or white matter integrity in a large imaging dataset from a single scanner of more than 4000 individuals. The sample sizes of MDD cases and controls included in the analyses of white matter integrity is by far the largest to our knowledge. Whilst we did not find any statistically significant subcortical volumetric differences between unaffected participants and individuals with probable MDD (using any of the definitions with increasing severity), we did find substantial evidence of reduced white matter integrity in MDD. This was seen globally, in two of the three categories of tracts (association and commissural fibres, and thalamic radiation tracts), and in individual tracts (bilateral superior thalamic radiations and left superior longitudinal fasciculus). Similar patterns of findings were seen for both principal and recurrent definition of depression with generally greater effect sizes in recurrent cases, with the exception of the localised differences in the superior thalamic radiation.

Our study notably did not find evidence for bilateral hippocampal volume reduction as previously reported in the large collaborative meta-analysis of MDD (32). We also did not find evidence of reductions in hippocampal volume when looking at recurrent MDD as published in the same review. The lack of subcortical volumetric differences associated with probable MDD diagnoses

in the current study therefore does not support the widely held belief that there are subcortical volumetric changes associated with the disorder. There are several potential explanations for this. Firstly, the UK Biobank dataset included only community-dwelling, ambulant individuals who could independently complete the health and cognitive assessments, and attend the follow-up imaging assessments. This approach arguably selected MDD groups that were more well/better functioning but equally more representative of the general population than purely clinically ascertained samples. We also used a composite 'probable' MDD diagnosis that was based on self-report symptoms and hospital admission statistics. In contrast, many other studies previously used a structured clinical interview schedule, such as the Structured Clinical Interview for DSM-IV (SCID), to define MDD according to standard criteria. Whilst the probable MDD definitions used in the current paper were not based on an interview, they showed many of the same epidemiological and risk-factor associations as clinically defined cases (34; 46).

Although we do not report subcortical volume differences, we did find substantive evidence for robust deficits in both global and local white matter integrity. We found that MDD patients had global loss of FA which was also found to be reduced in association and commissural fibres as well as in thalamic radiations, but not in projection fibres. FA in these structures was also more severely reduced in the recurrent MDD patients. The above results

indeed reflect previous findings from previous small-sample and meta-analytic studies (29; 47; 48), while extending them to a more generalizable population-based cohort excluding potential methodological confounds as associated with the previous studies. A previous meta-analytic study that compared 231 MDD patients with 261 healthy participants found reduced FA in inferior longitudinal fasciculus, inferior fronto-occipital fasciculus, posterior thalamic radiation and corpus callosum, which belong to the association/commissural fibres and thalamic radiations (29). Following the above study, another two recent meta-analyses found integrity reductions in the same categories, i.e. dorsal lateral PFC area, commissural fibres (48; 49). The global loss of FA in these regions could be the result of general neurodevelopmental alterations in MDD patients (23), and findings within defined subsets of white matter tracts could reflect the neurological basis of MDD as a disconnection within an integrated network of cortex-cortex and cortical-limbic pathways (50). The general FA reductions in groups of tracts is also consistent with findings from resting-state fMRI studies, which reported abnormalities in MDD populations in regional networks rather than just individual regions or structures (11; 51; 52). The networks that derive from prefrontal cortex and thalamus has been found largely contribute to emotional and social cognition processes (23). The reduced integrity in these groups of tracts may therefore reflect the repeatedly found impairment of emotion

regulation(53–55), reward processing (56; 57) and executive control (31) in MDD populations.

In the tests of single white matter tracts, we found significantly altered integrity in left superior longitudinal fasciculus both in the overall MDD population and to a greater extent in recurrent MDD patients. Reduction of integrity in superior thalamic radiation was also found in MDD compared with healthy subjects, however showed no specific change of FA in recurrent MDD.

Superior longitudinal fasciculus, as a part of association fibres, connects prefrontal cortex and other lobes (58). Small-sample studies have specifically reported reduced integrity in superior longitudinal fasciculus in various depressive samples, including elderly patients with depression (23; 59), depressive adolescents (60) and adolescents with familial risk for depression (58), compared with controls. Meta-analytic studies (48; 61) and a review (47) also ascertained that the reduction of white matter integrity specifically in superior longitudinal fasciculus may be an important biomarker of the presence of depression. A recent study combined genetic and neuroimaging techniques found that people with higher polygenic risk of depression have greater loss of FA in superior longitudinal fasciculus (62), suggesting that it may also therefore be a useful trait-related marker of risk. Loss of integrity in superior longitudinal fasciculus has also previously been reported to be

associated with various cognitive dysfunctions, like working memory (63) and attention (61). Severity of depressive symptoms was also found correlate with FA loss in superior longitudinal fasciculus (64). There is increasingly convincing evidence therefore that reduced integrity in superior longitudinal fasciculus might be an important feature of the neurobiology of MDD and may underlie impaired emotional process and cognitive abilities in MDD population (30).

Two potential limitations of the current study should be considered, these include the absence of a structured diagnostic interview schedule and the lack of hospital-based sampling. The large sample size may, however, overcome some of these difficulties and community based population sampling may yield more generalizable findings than those based on clinically ascertained samples alone (12; 65; 66). The current investigation, by avoiding the combination of clinically and methodologically diverse samples, may also have ameliorated several important confounds. The second limitation is that for the volumetric analysis we only focused on the subcortical volumes in the current study. We can therefore not exclude the possibility of cortical differences in MDD, including regional volume differences, as well as measures of cortical thickness and gyrification for example.

Our study presents a comprehensive comparison of brain structural changes related to MDD using the largest single sample available to date

from a single scanner with uniform methodologies for clinical categorisation and scanning. We mainly report reductions of white matter FA in general latent measures of association and commissural fibres as well as thalamic radiations, and in left superior longitudinal fasciculus both in MDD and recurrent MDD. Future work would be potentially focusing on structural changes in cortical areas as well as richer stratification of MDD into informative biologically-based subgroups.

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Conflicts of Interest

AMM has previously received grant support from Pfizer, Lilly and Janssen. These studies are not connected to the current investigation. Remaining authors report no conflicts of interest.

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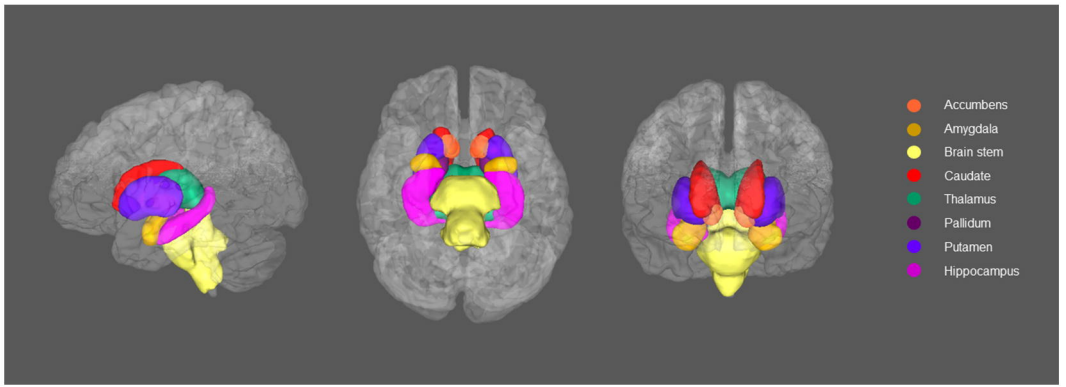
Figure legends

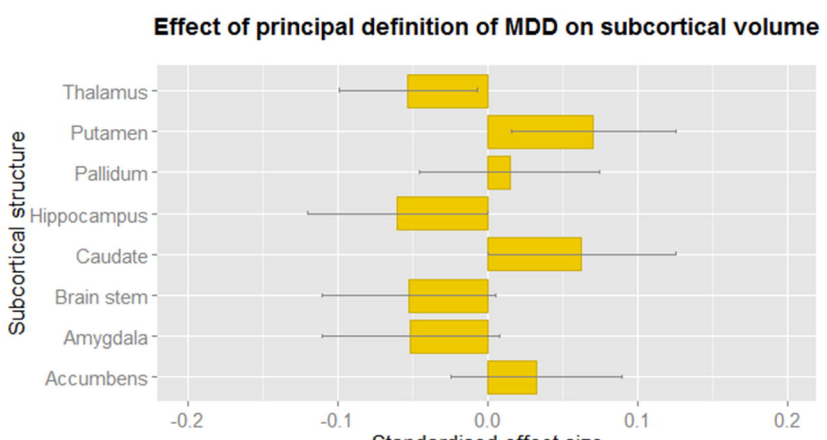
Figure 1. (A) Subcortical structures of interest in left, inferior and anterior view. (B) The effect of principal definition of probable MDD on subcortical volumes. Linear models were conducted, controlling the effect of age, age^2, sex and intracranial volume (and hemisphere for the regions that have bilateral values). The x-axis shows the standardised effect size of MDD definition, and y-axis is the layout of the subcortical structures. The error bar represents standard deviation of mean.

Figure 2. (A) White matter tracts in each anatomical subset in left, posterior and anterior view. (B) The effect of principal definition of probable MDD on FA value of tracts. Linear models were conducted, controlling the effect of age, age^2 and sex (and hemisphere for the tracts that have bilateral values). Left superior longitudinal fasciculus was presented because there was a significant interaction between recurrent MDD definition and hemisphere. Follow-up analysis showed a lateral effect of probable MDD definition on left superior longitudinal fasciculus. The x-axis shows the standardised effect size of MDD definition, and y-axis is the layout of the white matter tracts. The error bar represents standard deviation of mean.

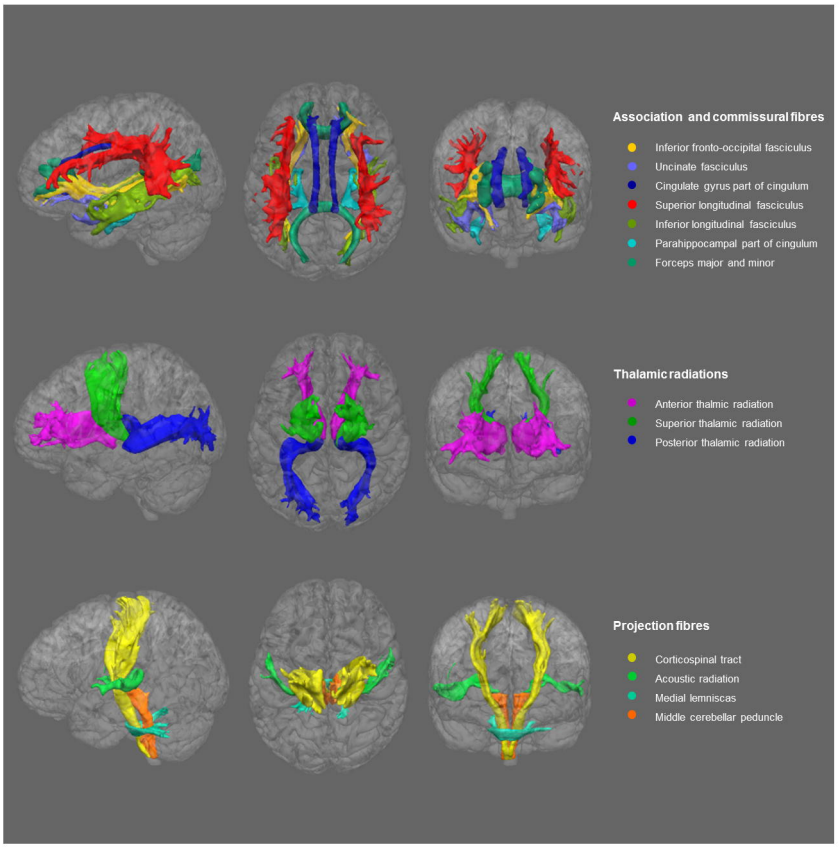
(A)


Accumbens
Amygdala
Brain stem
Caudate
Thalamus
Pallidum
Putamen
Hippocampus

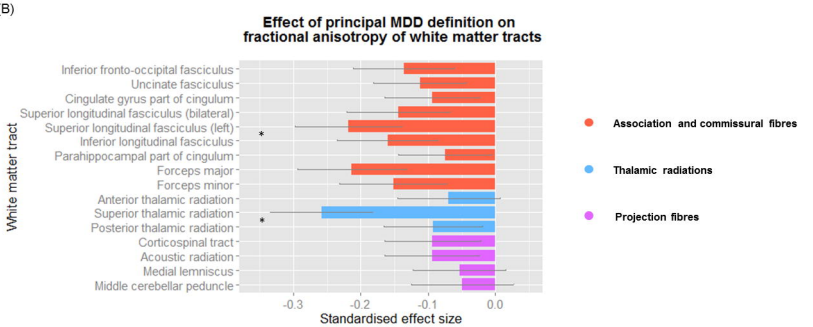
(B)


Effect of principal definition of MDD on subcortical volume
Subcortical structure
Thalamus
Putamen
Pallidum
Hippocampus
Caudate
Brain stem
Amygdala
Accumbens
-0.2
-0.1
0.0
0.1
0.2
Standardised effect size

(A)


Association and commissural fibres
Inferior fronto-occipital fasciculus
Uncinate fasciculus
Cingulate gyrus part of cingulum
Superior longitudinal fasciculus
Inferior longitudinal fasciculus
Parahippocampal part of cingulum
Forceps major and minor
Thalamic radiations
Anterior thalmic radiation
Superior thalamic radiation
Posterior thalamic radiation
Projection fibres
Corticospinal tract
Acoustic radiation
Medial lemniscas
Middle cerebellar peduncle

(B)


Effect of principal MDD definition on fractional anisotropy of white matter tracts
White matter tract
Inferior fronto-occipital fasciculus
Uncinate fasciculus
Cingulate gyrus part of cingulum
Superior longitudinal fasciculus (bilateral)
Superior longitudinal fasciculus (left)
Inferior longitudinal fasciculus
Parahippocampal part of cingulum
Forceps major
Forceps minor
Anterior thalamic radiation
Superior thalamic radiation
Posterior thalamic radiation
Corticospinal tract
Acoustic radiation
Medial lemniscus
Middle cerebellar peduncle
*
*
-0.3
-0.2
-0.1
0.0
Standardised effect size
Association and commissural fibres
Thalamic radiations
Projection fibres