Brain Structure in Chronic Pain and Depression Supplementary Material

# Table of contents:

## 1. Supplementary Methods

### 1.1. Neurological disorders excluded

### 1.2. Brain structures full details

## 2. Supplementary Results

### 2.1. Full results from main analysis

# 1. Supplementary Methods

## 1.1. Neurological disorders excluded

Neurological disorder status was determined based on self-reported illnesses recorded in UK Biobank data fields 20001 and 20002.

| Disorder | Data.field |
| --- | --- |
| Benign neuroma | 1683 |
| Brain abscess/intracranial abscess | 1245 |
| Brain haemorrhage | 1491 |
| Cerebral aneurysm | 1425 |
| Cerebral palsy | 1433 |
| Chronic/degenerative neurological problem | 1258 |
| dementia/alzheimers/cognitive impairment | 1263 |
| Encephalitis | 1246 |
| Epilepsy | 1264 |
| Fracture skull/head | 1626 |
| Head injury | 1266 |
| Ischaemic stroke | 1583 |
| Meningitis | 1247 |
| Motor Neurone Disease | 1259 |
| Multiple Sclerosis | 1261 |
| Nervous system infection | 1244 |
| Neurological injury/trauma | 1240 |
| Other demyelinating disease (not Multiple Sclerosis) | 1397 |
| Other neurological problem | 1434 |
| Parkinson’s Disease | 1262 |
| Spina Bifida | 1524 |
| Stroke | 1081 |
| Subarachnoid haemorrhage | 1086 |
| Subdural haemorrhage/haematoma | 1083 |
| Transient ischaemic attack | 1082 |
| Meningioma/benign meningeal tumour | 1659 |

Supplementary Table 1 Non-cancer neurological conditions excluded for based on data field 20002.

| Disorder | Data.field |
| --- | --- |
| Brain cancer/primary malignant brain tumour | 1032 |
| Meningeal cancer/malignant meningioma | 1031 |

Supplementary Table 2 Cancer neurological conditions excluded for based on data field 20001.

## 1.2. Brain structures full details

Measures of cortical volume, thickness and surface area in UK Biobank

| Cortical Region | Lobe |
| --- | --- |
| superior frontal gyrus | frontal |
| rostral middle frontal | frontal |
| caudal middle frontal | frontal |
| pars orbitalis | frontal |
| pars triangularis | frontal |
| pars opercularis | frontal |
| frontal pole | frontal |
| lateral orbitofrontal | frontal |
| precentral gyrus | frontal |
| paracentral cortex | frontal |
| insula | temporal |
| superior temporal | temporal |
| transverse temporal | temporal |
| banks STS | temporal |
| middle temporal gyrus | temporal |
| iferior temporal gyrus | temporal |
| fusiform | temporal |
| parahippocampal | temporal |
| entorhinal | temporal |
| postcentral gyrus | parietal |
| paracentral cortex | parietal |
| superior parietal cortex | parietal |
| inferior parietal cortex | parietal |
| supramarginal gyrus | parietal |
| precuneus | parietal |
| lateral occipital cortex | occipital |
| cuneus | occipital |
| pericalcarine cortex | occipital |
| lingual gyrus | occipital |
| rostral ACC | cingulate |
| caudal ACC | cingulate |
| posterior cingulate cortex | cingulate |
| cingulate isthmus | cingulate |

Supplementary Table 3 Cortical regions in UK Biobank and cortical lobes derived from “Desikan-Killiany-Tourville” atlas

| Subcortical Region |
| --- |
| thalamus |
| caudate |
| putamen |
| pallidum |
| hippocampus |
| amygdala |
| accumbens |

Supplementary Table 4 Regional Subcortical Volumes in UK Biobank derived using FIRST (FMRIB’s Integrated Registration and Segmentation Tool)

| White Matter Tract | General Measure |
| --- | --- |
| cingulate gyrus part of cingulum | association fibre |
| inferior fronto-occipital fasciculus | association fibre |
| inferior longitudinal fasciculus | association fibre |
| parahippocampal part of cingulum | association fibre |
| superior longitudinal fasciculus | association fibre |
| uncinate fasciculus | association fibre |
| forceps major | association fibre |
| forceps minor | association fibre |
| anterior thalamic radiation | thalamic radiations |
| posterior thalamic radiation | thalamic radiations |
| superior thalamic radiation | thalamic radiations |
| acoustic radiation | projection fibres |
| corticospinal tract | projection fibres |
| medial lemniscus | projection fibres |
| middle cerebellar peduncle | projection fibres |

Supplementary Table 5 White matter tracts in UK Biobank and general measures derived using AutoPtx.

| White Matter General Measures | Variance Explained |
| --- | --- |
| MD global | 0.438 |
| MD association fibres | 0.487 |
| MD projection fibres | 0.397 |
| MD thalamic associations | 0.739 |
| FA global | 0.415 |
| FA association fibres | 0.467 |
| FA projection fibres | 0.455 |
| FA thalamic associations | 0.651 |

Supplementary Table 6 Variance explained by the first principal component analysis (PCA) component for each global and general measure of white matter tracts.

## 2. Supplementary Results

### 2.1. Full results from analysis

| Brain Strucutre Phenotype | Full Sample Beta | Sex Interaction (Females - Males) | Female Sample Beta | Male Sample Beta |
| --- | --- | --- | --- | --- |
| Regional Subcortical Volume of accumbens | -0.017 | -0.006 |  |  |
| Regional Subcortical Volume of amygdala | 0.002 | -0.015 |  |  |
| Regional Subcortical Volume of caudate | 0.016 | -0.008 |  |  |
| Regional Subcortical Volume of hippocampus | -0.015 | -0.026 |  |  |
| Regional Subcortical Volume of pallidum | -0.008 | 0.01 |  |  |
| Regional Subcortical Volume of putamen | -0.016 | 0.006 |  |  |
| Regional Subcortical Volume of thalamus | -0.002 | -0.003 |  |  |
| Volume of bankssts | **-0.026\*\*\*** | -0.018 |  |  |
| Volume of caudalanteriorcingulate | **-0.016\*** | -0.013 |  |  |
| Volume of caudalmiddlefrontal | -0.012 | 0.009 |  |  |
| Volume of cuneus | 0.01 | 0.004 |  |  |
| Volume of entorhinal | **-0.022\*** | 0.015 |  |  |
| Volume of frontalpole |  | 0.028 |  |  |
| Volume of frontalpole left | **-0.028\*\*** |  |  |  |
| Volume of frontalpole right | 0.002 |  |  |  |
| Volume of fusiform | **-0.033\*\*\*** | -0.022 |  |  |
| Volume of inferiorparietal | **-0.029\*\*\*** | 0.01 |  |  |
| Volume of inferiortemporal | **-0.038\*\*\*** | -0.005 |  |  |
| Volume of insula | **-0.039\*\*\*** | 0.015 |  |  |
| Volume of isthmuscingulate | -0.003 | -0.002 |  |  |
| Volume of lateraloccipital | -0.005 | 0.004 |  |  |
| Volume of lateralorbitofrontal | **-0.02\*\*** | -0.003 |  |  |
| Volume of lingual | 0.006 | -0.002 |  |  |
| Volume of medialorbitofrontal | **-0.041\*\*\*** | -0.012 |  |  |
| Volume of middletemporal | **-0.032\*\*\*** | -0.005 |  |  |
| Volume of paracentral | **-0.022\*\*** | -0.021 |  |  |
| Volume of parahippocampal | -0.015 | 0.006 |  |  |
| Volume of parsopercularis | **-0.026\*\*** | 0.01 |  |  |
| Volume of parsorbitalis | 0.01 | -0.006 |  |  |
| Volume of parstriangularis | -0.012 | 0.006 |  |  |
| Volume of pericalcarine | 0.005 | -0.001 |  |  |
| Volume of postcentral | **-0.043\*\*\*** | 0.008 |  |  |
| Volume of posteriorcingulate | **-0.039\*\*\*** | -0.008 |  |  |
| Volume of precentral | **-0.026\*\*\*** | -0.001 |  |  |
| Volume of precuneus | -0.008 | -0.008 |  |  |
| Volume of rostralanteriorcingulate | **-0.029\*\*\*** | **-0.036\*** | **-0.044\*\*\*** | -0.008 |
| Volume of rostralmiddlefrontal | -0.009 | -0.007 |  |  |
| Volume of superiorfrontal | **-0.017\*\*** | 0.003 |  |  |
| Volume of superiorparietal | -0.006 | 0.004 |  |  |
| Volume of superiortemporal | **-0.025\*\*\*** | -0.007 |  |  |
| Volume of supramarginal | **-0.022\*\*** | -0.011 |  |  |
| Volume of transversetemporal | **-0.02\*** | 0.026 |  |  |
| Area of cingulate lobe | **-0.018\*\*** | -0.016 |  |  |
| Area of frontal lobe | **-0.023\*\*\*** | -0.005 |  |  |
| Area of global cortical | **-0.031\*\*\*** | -0.013 |  |  |
| Area of occipital lobe | **-0.02\*\*** | -0.018 |  |  |
| Area of parietal lobe | **-0.04\*\*\*** | -0.017 |  |  |
| Area of temporal lobe | **-0.029\*\*\*** | -0.011 |  |  |
| Area of bankssts | **-0.027\*\*\*** | -0.024 |  |  |
| Area of caudalanteriorcingulate | -0.012 | -0.012 |  |  |
| Area of caudalmiddlefrontal | -0.015 | 0.003 |  |  |
| Area of cuneus | -0.008 | -0.02 |  |  |
| Area of entorhinal | -0.012 | -0.005 |  |  |
| Area of frontalpole | -0.01 | 0.007 |  |  |
| Area of fusiform | **-0.029\*\*\*** | -0.022 |  |  |
| Area of inferiorparietal | **-0.036\*\*\*** | -0.005 |  |  |
| Area of inferiortemporal | **-0.037\*\*\*** | -0.01 |  |  |
| Area of insula | -0.01 | 0.015 |  |  |
| Area of isthmuscingulate | 0.007 | -0.009 |  |  |
| Area of lateraloccipital | **-0.021\*\*** | -0.017 |  |  |
| Area of lateralorbitofrontal | **-0.015\*** | -0.02 |  |  |
| Area of lingual | -0.017 | -0.019 |  |  |
| Area of medialorbitofrontal | **-0.023\*\*\*** | -0.007 |  |  |
| Area of middletemporal | **-0.035\*\*\*** | -0.012 |  |  |
| Area of paracentral | -0.007 | -0.019 |  |  |
| Area of parahippocampal | -0.004 | -0.002 |  |  |
| Area of parsopercularis | **-0.024\*\*** |  |  |  |
| Area of parsopercularis left |  | 0.034 |  |  |
| Area of parsopercularis right |  | -0.017 |  |  |
| Area of parsorbitalis | -0.004 | -0.016 |  |  |
| Area of parstriangularis | -0.014 | -0.001 |  |  |
| Area of pericalcarine | -0.013 | 0 |  |  |
| Area of postcentral | **-0.054\*\*\*** | -0.003 |  |  |
| Area of posteriorcingulate | **-0.025\*\*\*** | -0.005 |  |  |
| Area of precentral | **-0.021\*\*** | -0.002 |  |  |
| Area of precuneus | **-0.024\*\*\*** | **-0.031\*** | **-0.038\*\*\*** | -0.006 |
| Area of rostralanteriorcingulate | **-0.02\*\*** | -0.025 |  |  |
| Area of rostralmiddlefrontal | **-0.018\*\*** | -0.013 |  |  |
| Area of superiorfrontal | **-0.017\*** | -0.001 |  |  |
| Area of superiorparietal | **-0.029\*\*\*** | -0.008 |  |  |
| Area of superiortemporal | **-0.015\*** | -0.008 |  |  |
| Area of supramarginal | **-0.025\*\*\*** | -0.019 |  |  |
| Area of transversetemporal | -0.013 | 0.021 |  |  |
| Thickness of bankssts | -0.01 | 0.009 |  |  |
| Thickness of caudalanteriorcingulate | -0.008 | -0.007 |  |  |
| Thickness of caudalmiddlefrontal | 0.002 | 0.017 |  |  |
| Thickness of cuneus | **0.031\*\*** | **0.043\*** | **0.051\*\*\*** | 0.007 |
| Thickness of entorhinal | **-0.02\*** | 0.014 |  |  |
| Thickness of frontalpole | -0.008 | **0.035\*** | 0.009 | -0.026 |
| Thickness of fusiform | **-0.025\*** | -0.007 |  |  |
| Thickness of inferiorparietal | 0.013 | 0.034 |  |  |
| Thickness of inferiortemporal |  | 0.002 |  |  |
| Thickness of inferiortemporal left | **-0.036\*\*** |  |  |  |
| Thickness of inferiortemporal right | 0.001 |  |  |  |
| Thickness of insula |  | -0.001 |  |  |
| Thickness of insula left | **-0.053\*\*\*** |  |  |  |
| Thickness of insula right | **-0.031\*\*** |  |  |  |
| Thickness of isthmuscingulate | **-0.021\*** | 0.016 |  |  |
| Thickness of lateraloccipital | **0.031\*\*** | 0.034 |  |  |
| Thickness of lateralorbitofrontal | -0.008 | 0.023 |  |  |
| Thickness of lingual | **0.028\*\*** | 0.023 |  |  |
| Thickness of medialorbitofrontal | **-0.027\*\*** | -0.025 |  |  |
| Thickness of middletemporal | -0.011 | -0.008 |  |  |
| Thickness of paracentral | -0.012 | -0.002 |  |  |
| Thickness of parahippocampal | **-0.025\*** | 0.008 |  |  |
| Thickness of parsopercularis | -0.014 | 0.001 |  |  |
| Thickness of parsorbitalis | 0.017 | 0.013 |  |  |
| Thickness of parstriangularis | -0.001 | 0.023 |  |  |
| Thickness of pericalcarine | **0.036\*\*\*** | 0.011 |  |  |
| Thickness of postcentral | 0.001 | 0.018 |  |  |
| Thickness of posteriorcingulate | **-0.028\*\*** | -0.009 |  |  |
| Thickness of precentral | -0.007 | 0.008 |  |  |
| Thickness of precuneus | **0.031\*\*** | **0.044\*** | **0.051\*\*\*** | 0.007 |
| Thickness of rostralanteriorcingulate | **-0.021\*** | **-0.039\*** | **-0.038\*\*\*** | 0.002 |
| Thickness of rostralmiddlefrontal | 0.01 | 0.019 |  |  |
| Thickness of superiorfrontal | -0.003 | 0.01 |  |  |
| Thickness of superiorparietal | **0.049\*\*\*** | 0.035 |  |  |
| Thickness of superiortemporal | **-0.028\*\*** | -0.006 |  |  |
| Thickness of supramarginal | 0.003 | 0.023 |  |  |
| Thickness of transversetemporal | -0.013 | 0.01 |  |  |
| Thickness of cingulate lobe | **-0.033\*\*** | -0.016 |  |  |
| Thickness of frontal lobe | -0.006 | 0.012 |  |  |
| Thickness of global cortical | 0 | 0.019 |  |  |
| Thickness of occipital lobe | **0.039\*\*\*** | 0.036 |  |  |
| Thickness of parietal lobe | **0.022\*** | 0.033 |  |  |
| Thickness of temporal lobe | **-0.038\*\*\*** | -0.003 |  |  |
| FA in acoustic radiation | **0.022\*** | 0.01 |  |  |
| FA in anterior thalamic radiation | -0.011 | -0.019 |  |  |
| FA in cingulate gyrus part of cingulum | 0.007 | -0.022 |  |  |
| FA in corticospinal tract | 0.009 | 0.016 |  |  |
| FA in forceps major | -0.009 | 0.003 |  |  |
| FA in forceps minor | **-0.03\*\*** | 0.002 |  |  |
| FA in inferior fronto occipital fasciculus | -0.012 | 0 |  |  |
| FA in inferior longitudinal fasciculus | -0.002 | 0.011 |  |  |
| FA in medial lemniscus | 0.001 | 0.021 |  |  |
| FA in middle cerebellar peduncle | **0.023\*** | 0.001 |  |  |
| FA in parahippocampal part of cingulum | 0.019 | -0.016 |  |  |
| FA in posterior thalamic radiation | **-0.027\*** | 0.005 |  |  |
| FA in superior longitudinal fasciculus | -0.021 | -0.016 |  |  |
| FA in superior thalamic radiation | 0.018 | -0.012 |  |  |
| FA in uncinate fasciculus | -0.004 | 0.015 |  |  |
| FA in association fibres | -0.004 | -0.008 |  |  |
| FA in global | -0.001 | -0.003 |  |  |
| FA in projection fibres | 0.019 | 0.019 |  |  |
| FA in thalamic radiations | -0.012 | -0.009 |  |  |
| MD in acoustic radiation |  | -0.016 |  |  |
| MD in acoustic radiation left | 0.009 |  |  |  |
| MD in acoustic radiation right | **-0.032\*\*** |  |  |  |
| MD in anterior thalamic radiation | 0.002 | 0.003 |  |  |
| MD in cingulate gyrus part of cingulum | -0.002 | -0.006 |  |  |
| MD in corticospinal tract | -0.005 | -0.013 |  |  |
| MD in forceps major | -0.013 | **-0.05\*\*** | **-0.035\*\*** | 0.016 |
| MD in forceps minor | -0.007 | -0.003 |  |  |
| MD in inferior fronto occipital fasciculus | -0.013 | -0.025 |  |  |
| MD in inferior longitudinal fasciculus | -0.017 | -0.017 |  |  |
| MD in medial lemniscus | **-0.032\*\*** | -0.023 |  |  |
| MD in middle cerebellar peduncle | 0.011 | 0.013 |  |  |
| MD in parahippocampal part of cingulum | -0.012 | 0.01 |  |  |
| MD in posterior thalamic radiation | -0.006 | -0.009 |  |  |
| MD in superior longitudinal fasciculus | 0.003 | -0.012 |  |  |
| MD in superior thalamic radiation | -0.004 | 0.001 |  |  |
| MD in uncinate fasciculus | 0.009 | -0.016 |  |  |
| MD in association fibres | -0.012 | -0.014 |  |  |
| MD in global | -0.01 | -0.011 |  |  |
| MD in projection fibres | -0.009 | -0.001 |  |  |
| MD in thalamic radiations | -0.003 | -0.004 |  |  |
| Volume of frontal lobe | **-0.023\*\*\*** | -0.001 |  |  |

Supplementary Table 7 Full results for association and sex-interaction analysis between brain structure and chronic pain in full, female and male sample. \*, \*\* and \*\*\* represent significant results at pFDR<.05, pFDR<.01 and pFDR<.001, respectively (FDR correction not applied to p-values from sex-interaction analysis). Significant results are highlighted in bold.

| Brain Strucutre Phenotype | Full Sample Beta | Sex Interaction (Females - Males) | Female Sample Beta | Male Sample Beta |
| --- | --- | --- | --- | --- |
| Regional Subcortical Volume of accumbens | -0.011 | 0.014 |  |  |
| Regional Subcortical Volume of amygdala | 0.038 | -0.011 |  |  |
| Regional Subcortical Volume of caudate | 0.012 | -0.059 |  |  |
| Regional Subcortical Volume of hippocampus | 0.011 | -0.009 |  |  |
| Regional Subcortical Volume of pallidum | -0.014 | 0.008 |  |  |
| Regional Subcortical Volume of putamen | 0.002 | **-0.08\*** | -0.018 | **0.061\*** |
| Regional Subcortical Volume of thalamus | -0.03 | -0.011 |  |  |
| Volume of bankssts | -0.01 | -0.028 |  |  |
| Volume of caudalanteriorcingulate | -0.016 | 0.006 |  |  |
| Volume of caudalmiddlefrontal | -0.034 | 0.002 |  |  |
| Volume of cuneus | -0.007 | 0.049 |  |  |
| Volume of entorhinal | -0.017 | -0.005 |  |  |
| Volume of frontalpole | -0.03 | 0.042 |  |  |
| Volume of fusiform | -0.019 | -0.008 |  |  |
| Volume of inferiorparietal | -0.034 | -0.035 |  |  |
| Volume of inferiortemporal | -0.023 | 0.014 |  |  |
| Volume of insula | **-0.055\*\*** | 0.014 |  |  |
| Volume of isthmuscingulate | 0.004 | 0.003 |  |  |
| Volume of lateraloccipital | 0.006 | -0.006 |  |  |
| Volume of lateralorbitofrontal | -0.012 | 0.016 |  |  |
| Volume of lingual | -0.003 | -0.008 |  |  |
| Volume of medialorbitofrontal | -0.029 | 0.007 |  |  |
| Volume of middletemporal | -0.022 | -0.036 |  |  |
| Volume of paracentral | **-0.047\*** | -0.008 |  |  |
| Volume of parahippocampal | -0.013 | **0.079\*** | 0.016 | **-0.063\*** |
| Volume of parsopercularis | -0.025 | -0.016 |  |  |
| Volume of parsorbitalis | 0.017 | 0.023 |  |  |
| Volume of parstriangularis | -0.016 | -0.015 |  |  |
| Volume of pericalcarine | -0.013 | 0.051 |  |  |
| Volume of postcentral | -0.032 | -0.015 |  |  |
| Volume of posteriorcingulate | -0.03 | 0.017 |  |  |
| Volume of precentral | **-0.047\*** | 0.029 |  |  |
| Volume of precuneus | -0.011 | 0.004 |  |  |
| Volume of rostralanteriorcingulate | -0.007 | -0.029 |  |  |
| Volume of rostralmiddlefrontal | -0.017 | -0.005 |  |  |
| Volume of superiorfrontal | -0.024 | 0.001 |  |  |
| Volume of superiorparietal | -0.016 | 0.027 |  |  |
| Volume of superiortemporal | 0 | -0.008 |  |  |
| Volume of supramarginal | -0.022 | -0.024 |  |  |
| Volume of transversetemporal | 0.007 | -0.049 |  |  |
| Area of cingulate lobe | 0.005 | -0.021 |  |  |
| Area of frontal lobe | -0.007 | -0.009 |  |  |
| Area of global cortical | -0.009 | -0.016 |  |  |
| Area of occipital lobe | -0.014 | 0.009 |  |  |
| Area of parietal lobe | -0.016 | -0.021 |  |  |
| Area of temporal lobe | 0.001 | -0.033 |  |  |
| Area of bankssts | -0.001 | -0.044 |  |  |
| Area of caudalanteriorcingulate | 0.005 | -0.006 |  |  |
| Area of caudalmiddlefrontal | -0.022 | 0.007 |  |  |
| Area of cuneus | -0.02 | 0.054 |  |  |
| Area of entorhinal | 0.003 | -0.034 |  |  |
| Area of frontalpole |  | 0.01 |  |  |
| Area of frontalpole left | 0.008 |  |  |  |
| Area of frontalpole right | -0.03 |  |  |  |
| Area of fusiform | 0.002 | -0.044 |  |  |
| Area of inferiorparietal | -0.023 | -0.056 |  |  |
| Area of inferiortemporal | 0.002 | -0.006 |  |  |
| Area of insula | -0.021 | 0.009 |  |  |
| Area of isthmuscingulate | 0.019 | -0.026 |  |  |
| Area of lateraloccipital | 0.002 | -0.028 |  |  |
| Area of lateralorbitofrontal | 0.022 | -0.004 |  |  |
| Area of lingual | -0.019 | 0.01 |  |  |
| Area of medialorbitofrontal | 0.02 | -0.037 |  |  |
| Area of middletemporal | 0.002 | -0.039 |  |  |
| Area of paracentral | -0.005 | -0.009 |  |  |
| Area of parahippocampal | 0.006 | -0.009 |  |  |
| Area of parsopercularis | -0.008 | -0.033 |  |  |
| Area of parsorbitalis | 0.04 | -0.024 |  |  |
| Area of parstriangularis | -0.001 | -0.028 |  |  |
| Area of pericalcarine | -0.025 | 0.045 |  |  |
| Area of postcentral | -0.021 | -0.01 |  |  |
| Area of posteriorcingulate | -0.012 |  |  |  |
| Area of posteriorcingulate left |  | 0.064 |  |  |
| Area of posteriorcingulate right |  | -0.047 |  |  |
| Area of precentral | -0.017 | 0.025 |  |  |
| Area of precuneus | 0.002 | 0.003 |  |  |
| Area of rostralanteriorcingulate | 0.005 | -0.041 |  |  |
| Area of rostralmiddlefrontal | -0.004 | -0.027 |  |  |
| Area of superiorfrontal | -0.001 | -0.003 |  |  |
| Area of superiorparietal | -0.016 | 0.022 |  |  |
| Area of superiortemporal | 0.01 | -0.026 |  |  |
| Area of supramarginal | -0.006 | -0.035 |  |  |
| Area of transversetemporal | 0.006 | -0.04 |  |  |
| Thickness of bankssts | -0.038 | 0.043 |  |  |
| Thickness of caudalanteriorcingulate | -0.026 | 0.02 |  |  |
| Thickness of caudalmiddlefrontal | -0.034 | -0.015 |  |  |
| Thickness of cuneus | 0.02 | 0.005 |  |  |
| Thickness of entorhinal | -0.028 | 0.047 |  |  |
| Thickness of frontalpole | -0.029 | 0.019 |  |  |
| Thickness of fusiform |  | 0.035 |  |  |
| Thickness of fusiform left | **-0.084\*\*** |  |  |  |
| Thickness of fusiform right | -0.019 |  |  |  |
| Thickness of inferiorparietal | -0.023 | 0.025 |  |  |
| Thickness of inferiortemporal | **-0.069\*\*** | 0.015 |  |  |
| Thickness of insula | -0.038 | -0.018 |  |  |
| Thickness of isthmuscingulate | -0.026 | 0.06 |  |  |
| Thickness of lateraloccipital | 0.01 | 0.037 |  |  |
| Thickness of lateralorbitofrontal | **-0.05\*** | 0.031 |  |  |
| Thickness of lingual | 0.011 | -0.012 |  |  |
| Thickness of medialorbitofrontal | **-0.058\*\*** | 0.048 |  |  |
| Thickness of middletemporal | **-0.06\*\*** | -0.005 |  |  |
| Thickness of paracentral | **-0.06\*\*** | -0.002 |  |  |
| Thickness of parahippocampal | -0.031 | **0.087\*** | -0.001 | **-0.088\*\*** |
| Thickness of parsopercularis | -0.041 | 0.043 |  |  |
| Thickness of parsorbitalis | -0.032 | 0.045 |  |  |
| Thickness of parstriangularis | -0.037 | 0.018 |  |  |
| Thickness of pericalcarine | 0.024 | 0.02 |  |  |
| Thickness of postcentral | -0.027 | -0.016 |  |  |
| Thickness of posteriorcingulate |  | -0.003 |  |  |
| Thickness of posteriorcingulate left | **-0.073\*\*** |  |  |  |
| Thickness of posteriorcingulate right | -0.001 |  |  |  |
| Thickness of precentral | **-0.053\*** | 0.018 |  |  |
| Thickness of precuneus | -0.025 | -0.019 |  |  |
| Thickness of rostralanteriorcingulate | -0.024 | 0.019 |  |  |
| Thickness of rostralmiddlefrontal | -0.032 | 0.046 |  |  |
| Thickness of superiorfrontal | **-0.053\*** | -0.002 |  |  |
| Thickness of superiorparietal | 0.005 | -0.016 |  |  |
| Thickness of superiortemporal | -0.022 | 0.018 |  |  |
| Thickness of supramarginal | -0.032 | 0.03 |  |  |
| Thickness of transversetemporal | -0.007 | 0.01 |  |  |
| Thickness of cingulate lobe | **-0.051\*** | 0.029 |  |  |
| Thickness of frontal lobe | **-0.058\*\*** | 0.028 |  |  |
| Thickness of global cortical | **-0.043\*** | 0.017 |  |  |
| Thickness of occipital lobe | 0.021 | 0.012 |  |  |
| Thickness of parietal lobe | -0.026 | -0.004 |  |  |
| Thickness of temporal lobe | **-0.062\*\*** | 0.025 |  |  |
| FA in acoustic radiation | -0.02 | -0.006 |  |  |
| FA in anterior thalamic radiation | -0.036 | -0.023 |  |  |
| FA in cingulate gyrus part of cingulum | **-0.051\*** | -0.057 |  |  |
| FA in corticospinal tract | -0.002 | 0.065 |  |  |
| FA in forceps major | **-0.054\*** | 0.019 |  |  |
| FA in forceps minor | **-0.062\*\*** | -0.032 |  |  |
| FA in inferior fronto occipital fasciculus | **-0.067\*\*** | -0.029 |  |  |
| FA in inferior longitudinal fasciculus | **-0.063\*\*** | 0.023 |  |  |
| FA in medial lemniscus |  | 0.015 |  |  |
| FA in medial lemniscus left | 0.003 |  |  |  |
| FA in medial lemniscus right | **-0.055\*** |  |  |  |
| FA in middle cerebellar peduncle | 0 | -0.013 |  |  |
| FA in parahippocampal part of cingulum | -0.016 | 0.012 |  |  |
| FA in posterior thalamic radiation | **-0.077\*\*\*** | 0.02 |  |  |
| FA in superior longitudinal fasciculus | -0.044 | -0.005 |  |  |
| FA in superior thalamic radiation | -0.041 | -0.034 |  |  |
| FA in uncinate fasciculus | -0.039 | -0.038 |  |  |
| FA in association fibres | **-0.07\*\*\*** | -0.028 |  |  |
| FA in global | **-0.063\*\*\*** | -0.011 |  |  |
| FA in projection fibres | -0.018 | 0.034 |  |  |
| FA in thalamic radiations | **-0.067\*\*\*** | -0.009 |  |  |
| MD in acoustic radiation | -0.001 | -0.009 |  |  |
| MD in anterior thalamic radiation | 0.033 | 0.019 |  |  |
| MD in cingulate gyrus part of cingulum | **0.043\*** | 0.023 |  |  |
| MD in corticospinal tract | 0.033 | 0.016 |  |  |
| MD in forceps major | **0.046\*** | 0.021 |  |  |
| MD in forceps minor | **0.048\*** | 0.029 |  |  |
| MD in inferior fronto occipital fasciculus | **0.047\*** | -0.003 |  |  |
| MD in inferior longitudinal fasciculus | 0.031 | -0.004 |  |  |
| MD in medial lemniscus | 0.002 | -0.032 |  |  |
| MD in middle cerebellar peduncle | **0.072\*\*\*** | 0.029 |  |  |
| MD in parahippocampal part of cingulum | 0.005 | -0.04 |  |  |
| MD in posterior thalamic radiation | **0.049\*** | -0.006 |  |  |
| MD in superior longitudinal fasciculus | **0.043\*** | 0.02 |  |  |
| MD in superior thalamic radiation | **0.058\*\*** | 0.014 |  |  |
| MD in uncinate fasciculus | 0.029 | 0.003 |  |  |
| MD in association fibres | **0.04\*** | -0.01 |  |  |
| MD in global | **0.05\*\*** | 0.003 |  |  |
| MD in projection fibres | **0.061\*\*** | 0.019 |  |  |
| MD in thalamic radiations | **0.052\*\*** | 0.007 |  |  |
| Volume of frontal lobe | **-0.033\*** | 0.006 |  |  |

Supplementary Table 8 Full results for chronic pain interaction and sex-chronic pain interaction analysis between brain structure and depression in full, female and male sample. \*, \*\* and \*\*\* represent significant results at pFDR<.05, pFDR<.01 and pFDR<.001, respectively (FDR correction not applied to p-values from sex-interaction analysis). Significant results are highlighted in bold.

| Brain Strucutre Phenotype | Full Sample Beta | Sex Interaction (Females - Males) | Female Sample Beta | Male Sample Beta |
| --- | --- | --- | --- | --- |
| Regional Subcortical Volume of accumbens | 0.011 | 0.01 |  |  |
| Regional Subcortical Volume of amygdala | -0.027 | -0.089 |  |  |
| Regional Subcortical Volume of caudate | -0.014 | -0.023 |  |  |
| Regional Subcortical Volume of hippocampus | -0.024 | 0.044 |  |  |
| Regional Subcortical Volume of pallidum | -0.005 | -0.002 |  |  |
| Regional Subcortical Volume of putamen | -0.021 | -0.058 |  |  |
| Regional Subcortical Volume of thalamus | -0.020 | -0.044 |  |  |
| Volume of bankssts | -0.017 |  |  |  |
| Volume of bankssts left |  | 0.032 |  |  |
| Volume of bankssts right |  | **-0.224\*\*** | -0.082 | 0.142 |
| Volume of caudalanteriorcingulate | 0.018 | -0.081 |  |  |
| Volume of caudalmiddlefrontal | -0.019 | 0.06 |  |  |
| Volume of cuneus | -0.051 | 0.108 |  |  |
| Volume of entorhinal | 0.002 | -0.038 |  |  |
| Volume of frontalpole | -0.046 | -0.073 |  |  |
| Volume of fusiform | -0.019 |  |  |  |
| Volume of fusiform left |  | 0.045 |  |  |
| Volume of fusiform right |  | **-0.156\*** | -0.057 | 0.099 |
| Volume of inferiorparietal | 0.015 | -0.069 |  |  |
| Volume of inferiortemporal | 0.020 | 0.014 |  |  |
| Volume of insula | -0.002 | 0.01 |  |  |
| Volume of isthmuscingulate | 0.006 | -0.042 |  |  |
| Volume of lateraloccipital | -0.018 | 0.049 |  |  |
| Volume of lateralorbitofrontal | -0.038 | -0.072 |  |  |
| Volume of lingual | -0.007 | -0.03 |  |  |
| Volume of medialorbitofrontal | -0.039 | -0.011 |  |  |
| Volume of middletemporal | -0.028 | 0.034 |  |  |
| Volume of paracentral | -0.027 | 0.095 |  |  |
| Volume of parahippocampal | -0.017 | 0.023 |  |  |
| Volume of parsopercularis | 0.009 | 0.022 |  |  |
| Volume of parsorbitalis | -0.024 | 0.013 |  |  |
| Volume of parstriangularis | -0.010 | -0.026 |  |  |
| Volume of pericalcarine | -0.056 | 0.089 |  |  |
| Volume of postcentral | -0.029 | -0.011 |  |  |
| Volume of posteriorcingulate | 0.010 | 0.024 |  |  |
| Volume of precentral | -0.032 | 0.015 |  |  |
| Volume of precuneus | -0.011 | -0.078 |  |  |
| Volume of rostralanteriorcingulate | 0.013 | -0.009 |  |  |
| Volume of rostralmiddlefrontal | -0.022 | 0.07 |  |  |
| Volume of superiorfrontal | -0.002 | 0.037 |  |  |
| Volume of superiorparietal | -0.010 | -0.073 |  |  |
| Volume of superiortemporal | -0.022 | 0.062 |  |  |
| Volume of supramarginal | 0.011 | -0.065 |  |  |
| Volume of transversetemporal | -0.001 | 0.083 |  |  |
| Area of cingulate lobe | 0.044 | -0.054 |  |  |
| Area of frontal lobe | 0.018 | 0.005 |  |  |
| Area of global cortical | 0.025 | -0.034 |  |  |
| Area of occipital lobe | -0.027 | 0.054 |  |  |
| Area of parietal lobe | 0.043 | **-0.114\*** | 0.013 | **0.127\*\*** |
| Area of temporal lobe | 0.037 | -0.036 |  |  |
| Area of bankssts | -0.006 |  |  |  |
| Area of bankssts left |  | 0.057 |  |  |
| Area of bankssts right |  | **-0.248\*\*** | -0.066 | **0.181\*** |
| Area of caudalanteriorcingulate | 0.038 | -0.076 |  |  |
| Area of caudalmiddlefrontal | 0.013 | 0.056 |  |  |
| Area of cuneus | -0.043 | **0.158\*** | 0.010 | **-0.148\*** |
| Area of entorhinal | 0.004 | -0.118 |  |  |
| Area of frontalpole | -0.020 | -0.052 |  |  |
| Area of fusiform | 0.012 | -0.058 |  |  |
| Area of inferiorparietal | 0.049 | -0.095 |  |  |
| Area of inferiortemporal | 0.044 | -0.009 |  |  |
| Area of insula | 0.040 | -0.034 |  |  |
| Area of isthmuscingulate | 0.020 | -0.039 |  |  |
| Area of lateraloccipital | -0.009 | 0.032 |  |  |
| Area of lateralorbitofrontal | 0.006 | -0.069 |  |  |
| Area of lingual | -0.016 | -0.02 |  |  |
| Area of medialorbitofrontal | 0.014 | -0.057 |  |  |
| Area of middletemporal | 0.011 | 0.005 |  |  |
| Area of paracentral | -0.015 | -0.041 |  |  |
| Area of parahippocampal | 0.023 | 0.008 |  |  |
| Area of parsopercularis | 0.060 | -0.065 |  |  |
| Area of parsorbitalis | -0.010 | 0.023 |  |  |
| Area of parstriangularis | 0.022 | -0.045 |  |  |
| Area of pericalcarine | -0.046 | 0.085 |  |  |
| Area of postcentral | 0.042 | -0.099 |  |  |
| Area of posteriorcingulate | 0.041 | 0.002 |  |  |
| Area of precentral | 0.023 | -0.058 |  |  |
| Area of precuneus | 0.018 | -0.081 |  |  |
| Area of rostralanteriorcingulate | 0.026 | -0.048 |  |  |
| Area of rostralmiddlefrontal | 0.001 | 0.064 |  |  |
| Area of superiorfrontal | 0.036 | 0.032 |  |  |
| Area of superiorparietal | 0.034 | -0.086 |  |  |
| Area of superiortemporal | 0.048 | -0.002 |  |  |
| Area of supramarginal | 0.036 | -0.1 |  |  |
| Area of transversetemporal | 0.062 | 0.013 |  |  |
| Thickness of bankssts | -0.042 | -0.075 |  |  |
| Thickness of caudalanteriorcingulate | -0.031 |  |  |  |
| Thickness of caudalanteriorcingulate left |  | 0.098 |  |  |
| Thickness of caudalanteriorcingulate right |  | **-0.197\*** | -0.107 | 0.09 |
| Thickness of caudalmiddlefrontal | -0.069 | 0.045 |  |  |
| Thickness of cuneus | -0.040 | -0.03 |  |  |
| Thickness of entorhinal | 0.015 | 0.088 |  |  |
| Thickness of frontalpole | -0.032 | 0.003 |  |  |
| Thickness of fusiform | -0.038 | 0.059 |  |  |
| Thickness of inferiorparietal | -0.064 | 0.05 |  |  |
| Thickness of inferiortemporal | -0.055 |  |  |  |
| Thickness of inferiortemporal left |  | **0.208\*** | 0.009 | **-0.199\*** |
| Thickness of inferiortemporal right |  | -0.102 |  |  |
| Thickness of insula | -0.040 |  |  |  |
| Thickness of insula left |  | **0.245\*\*** | 0.045 | **-0.199\*** |
| Thickness of insula right |  | -0.057 |  |  |
| Thickness of isthmuscingulate | 0.001 | 0.019 |  |  |
| Thickness of lateraloccipital | -0.032 | 0.072 |  |  |
| Thickness of lateralorbitofrontal | -0.073 | 0.018 |  |  |
| Thickness of lingual | 0.015 | -0.012 |  |  |
| Thickness of medialorbitofrontal | -0.088 |  |  |  |
| Thickness of medialorbitofrontal left |  | **0.249\*\*** | -0.001 | **-0.25\*\*** |
| Thickness of medialorbitofrontal right |  | -0.04 |  |  |
| Thickness of middletemporal | -0.056 | 0.069 |  |  |
| Thickness of paracentral | -0.020 | **0.162\*** | 0.036 | -0.126 |
| Thickness of parahippocampal | -0.038 | 0.034 |  |  |
| Thickness of parsopercularis | -0.078 | **0.154\*** | -0.030 | **-0.184\*** |
| Thickness of parsorbitalis | -0.052 | 0.035 |  |  |
| Thickness of parstriangularis | -0.081 | 0.05 |  |  |
| Thickness of pericalcarine | -0.020 | 0.045 |  |  |
| Thickness of postcentral | -0.100 | 0.074 |  |  |
| Thickness of posteriorcingulate | -0.045 | 0.035 |  |  |
| Thickness of precentral | -0.076 | 0.089 |  |  |
| Thickness of precuneus | -0.035 | 0.025 |  |  |
| Thickness of rostralanteriorcingulate | -0.016 | 0.068 |  |  |
| Thickness of rostralmiddlefrontal | -0.039 | 0 |  |  |
| Thickness of superiorfrontal | -0.053 | 0.045 |  |  |
| Thickness of superiorparietal | -0.076 | -0.008 |  |  |
| Thickness of superiortemporal | -0.084 | 0.13 |  |  |
| Thickness of supramarginal | -0.061 | 0.088 |  |  |
| Thickness of transversetemporal | -0.069 | 0.099 |  |  |
| Thickness of cingulate lobe | -0.039 | 0.033 |  |  |
| Thickness of frontal lobe | -0.077 | 0.087 |  |  |
| Thickness of global cortical | -0.071 | 0.085 |  |  |
| Thickness of occipital lobe | -0.017 | 0.028 |  |  |
| Thickness of parietal lobe | -0.076 | 0.06 |  |  |
| Thickness of temporal lobe | -0.078 | 0.133 |  |  |
| FA in acoustic radiation | 0.014 | 0.004 |  |  |
| FA in anterior thalamic radiation | 0.003 | 0.051 |  |  |
| FA in cingulate gyrus part of cingulum | 0.002 | -0.02 |  |  |
| FA in corticospinal tract | 0.020 | 0.025 |  |  |
| FA in forceps major | 0.018 | -0.003 |  |  |
| FA in forceps minor | 0.014 | -0.098 |  |  |
| FA in inferior fronto occipital fasciculus | -0.017 | -0.019 |  |  |
| FA in inferior longitudinal fasciculus | -0.013 | 0.027 |  |  |
| FA in medial lemniscus | -0.026 | -0.012 |  |  |
| FA in middle cerebellar peduncle | -0.007 | -0.078 |  |  |
| FA in parahippocampal part of cingulum | -0.013 | -0.088 |  |  |
| FA in posterior thalamic radiation | 0.025 | 0.005 |  |  |
| FA in superior longitudinal fasciculus | 0.009 | -0.059 |  |  |
| FA in superior thalamic radiation | -0.003 | -0.139 |  |  |
| FA in uncinate fasciculus | -0.034 | 0.085 |  |  |
| FA in association fibres | -0.007 | -0.027 |  |  |
| FA in global | 0.001 | -0.023 |  |  |
| FA in projection fibres | 0.006 | -0.011 |  |  |
| FA in thalamic radiations | 0.014 | -0.023 |  |  |
| MD in acoustic radiation | 0.002 | 0.087 |  |  |
| MD in anterior thalamic radiation | -0.003 | -0.018 |  |  |
| MD in cingulate gyrus part of cingulum | 0.004 | 0.035 |  |  |
| MD in corticospinal tract | 0.030 | 0.037 |  |  |
| MD in forceps major | -0.014 | 0.097 |  |  |
| MD in forceps minor | -0.023 | **0.163\*** | 0.027 | **-0.135\*** |
| MD in inferior fronto occipital fasciculus | -0.006 | 0.022 |  |  |
| MD in inferior longitudinal fasciculus | -0.011 | 0.042 |  |  |
| MD in medial lemniscus | -0.029 | -0.091 |  |  |
| MD in middle cerebellar peduncle | -0.024 | 0.11 |  |  |
| MD in parahippocampal part of cingulum | -0.034 | -0.021 |  |  |
| MD in posterior thalamic radiation | -0.025 | 0.047 |  |  |
| MD in superior longitudinal fasciculus | 0.005 | 0.06 |  |  |
| MD in superior thalamic radiation | 0.005 | 0.088 |  |  |
| MD in uncinate fasciculus | -0.003 | 0.011 |  |  |
| MD in association fibres | -0.022 | 0.039 |  |  |
| MD in global | -0.017 | 0.047 |  |  |
| MD in projection fibres | -0.021 | 0.066 |  |  |
| MD in thalamic radiations | -0.013 | 0.038 |  |  |
| Volume of frontal lobe | -0.024 | 0.035 |  |  |

Supplementary Table 9 Full results for chronic pain interaction and sex-chronic pain interaction on the association of depression and brain structure in full, female and male sample. \*, \*\* and \*\*\* represent significant results at pFDR<.05, pFDR<.01 and pFDR<.001, respectively, respectively (FDR correction not applied to p-values from sex-interaction analysis). Significant results are highlighted in bold.