

1 Connectomes for 40,000 UK Biobank participants: A 2 multi-modal, multi-scale brain network resource 3 (Dated: March 8, 2023)

4 **Sina Mansour L.^{1,*}, Maria A. Di Biase^{2, 3, 4}, Robert E. Smith^{5,6}, Andrew Zalesky^{1,2}, and Caio
5 Seguin^{2,7}**

6 ¹Department of Biomedical Engineering, The University of Melbourne, VIC, Australia

7 ²Melbourne Neuropsychiatry Centre, Department of Psychiatry, The University of Melbourne, Parkville, Victoria,
Australia

8 ³Department of Anatomy and Physiology, School of Biomedical Sciences, The University of Melbourne, Parkville,
Victoria, Australia

9 ⁴Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, MA, USA

10 ⁵The Florey Institute of Neuroscience and Mental Health, Heidelberg, Victoria, Australia

11 ⁶Florey Department of Neuroscience and Mental Health, The University of Melbourne, Parkville, Victoria, Australia

12 ⁷Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA

13 *To whom correspondence should be addressed. Email: sina.mansour.lakouraj@gmail.com

16 ABSTRACT

17 We mapped functional and structural brain networks for more than 40,000 UK Biobank participants. Structural connectivity was estimated with tractography and diffusion MRI. Resting-state functional MRI was used to infer regional functional connectivity. We provide high-quality structural and functional connectomes for multiple parcellation granularities, several alternative measures of interregional connectivity, and a variety of common data pre-processing techniques, yielding more than one million connectomes in total and requiring more than 200,000 hours of compute time. For a single subject, we provide 28 out-of-the-box versions of structural and functional brain networks, allowing users to select, e.g., the parcellation and connectivity measure that best suit their research goals. Furthermore, we provide code and intermediate data for the time-efficient reconstruction of more than 1,000 different versions of a subject's connectome based on an array of methodological choices. All connectomes are available via the UK Biobank data sharing platform and our connectome mapping pipelines are openly available. In this report, we describe our connectome resource in detail for users, outline key considerations in developing an efficient pipeline to map an unprecedented number of connectomes, and report on the quality control procedures that were completed to ensure connectome reliability and accuracy. We demonstrate that our structural and functional connectivity matrices meet a number of quality control checks and replicate previously established findings in network neuroscience. We envisage that our resource will enable new studies of the human connectome in health, disease and aging at an unprecedented scale.

18 Background & Summary

19 Different aspects of brain connectivity can be quantified using different MRI modalities: diffusion-weighted MRI data can be
20 utilized to map structural brain networks of white-matter connections^{1,2}; alternatively, functional MRI data can be used to map
21 functional connectivity networks describing inter-regional interactions in brain activity^{3,4}. These network representations of
22 brain connectivity are referred to as connectomes^{5,6}. Establishing a large-scale community biobank of structural and functional
23 human connectomes will enable a diverse range of research into brain networks in health and disease.

24 The importance of large-scale neuroimaging biobanks is increasingly recognized as key to addressing reproducibility
25 concerns in neuroscience^{7–12}. The UK biobank (UKB)—a population study containing in-depth biomedical, health, and
26 environmental data—is the world's largest neuroimaging resource (with ~45,000 imaging sessions acquired from ~40,000
27 participants thus far)^{8,13–15}. This biobank offers tremendous potential for research on early disease prediction and alignment
28 of image-derived phenotypes (IDPs) with cognitive, behavioral, genetic, and medical observations. The availability of
29 longitudinal neuroimaging data accompanying constantly updated clinical records enables prospective neuroscientific research
30 at a population scale. To facilitate this effort, the UKB has released a range of important quantitative neuroimaging derivatives,
31 including regional measures of brain structure, microstructure, and function. At present however, measures of brain *connectivity*
32 are not a part of this resource. Mapping connectomes from neuroimaging data at scale is computationally burdensome and

33 requires significant technical expertise. Establishing a brain connectivity biobank for the UKB will ensure rapid access
34 to connectomes for researchers without expertise or computing resources for large-scale connectivity mapping, facilitate
35 reproducible neuroscience practices, enhance UKB utilization among the research community and ultimately lead to new
36 discoveries about brain networks.

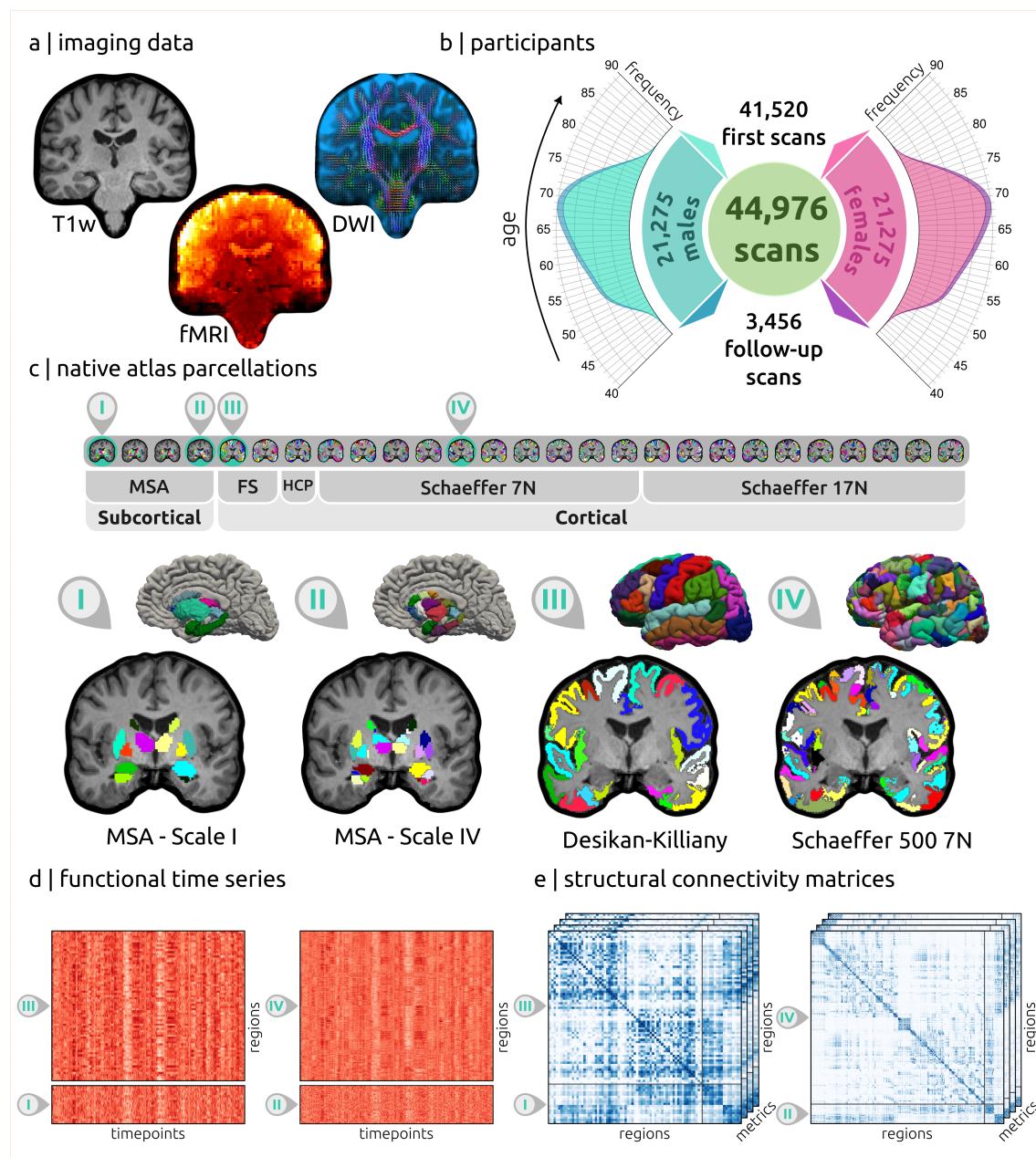


Figure 1. A comprehensive connectome biobank for the UK Biobank. (a) Structural and functional connectomes were mapped from diffusion and resting-state functional MRI data, respectively, while T1-weighted structural MRI was used for brain alignment. (b) Distribution of age and sex in the 41,520 UK Biobank participants with neuroimaging data available. Longitudinal data was available for 3,456 participants. (c) Various whole-brain atlases were used to map individual parcellations in native volumetric space. A total of 27 alternative parcellation schemes were computed. Four representative subcortical (I and II) and cortical (III and IV) parcellations of different granularities are illustrated. (d) Resting-state functional time series and (e) various structural connectivity matrices were computed for different parcellations. The time series and structural connectivity matrices are depicted for the same four sample parcellations. Abbreviations; MSA: Melbourne Subcortical Atlas, FS: FreeSurfer atlases, HCP: HCP-MMP1.0 atlas.

37 Here, we introduce our novel human connectome resource of brain atlases and connectivity matrices mapped for more than
38 40,000 adults participating in the UKB (see Figure 1). We provide functional activity time series and structural connectivity
39 matrices for multiple parcellation schemes, several alternative measures of interregional connectivity and a variety of common
40 data pre-processing techniques, yielding 27 brain-wide functional time series (enabling flexible and efficient access to various
41 functional connectivity metrics), and 28 structural connectomes per imaging session, and more than one million connectomes
42 and time-series in total. This required development of highly efficient connectome mapping pipelines and storage formats.
43 Connectivity data is made available in compact and easy-to-use data formats and our connectome mapping pipelines are openly
44 available. We completed extensive quality control procedures to ensure the accuracy and reliability of all connectivity matrices.
45 This report aims to describe our connectome resource in detail for prospective users, provide insight into the key considerations
46 that shaped the development of our connectome mapping pipeline and outline quality control procedures. We envisage that this
47 resource will be of high utility and complement the current IDPs available in the UKB.

48 Methods

49 UK Biobank data

50 Background

51 The UKB is a large-scale dataset comprising over 500,000 participants (aged 40-69 years). The biobank is publicly available
52 to advance health-related research¹³. Importantly, access to full health records (which are updated over time), and a wide
53 range of longitudinal, long-term clinical, phenotypic, and genomic data is available to researchers¹⁵. In addition, UKB aims to
54 acquire longitudinal neuroimaging data for 100,000 participants, with ~45,000 separate MRI sessions for ~40,000 participants
55 released thus far^{8,14}.

56 Participants

57 Brain MRI data sourced for the connectome biobank consists of 44,976 separate imaging sessions (23,701 females and 21,275
58 males) from 41,520 individuals (21,951 females and 19,569 males) aged 44–82 years ($\mu = 64.0$, $\sigma = 7.6$ years) at time of
59 acquisition. For 3,456 individuals (1,750 females and 1,706 males) a single longitudinal follow-up MRI session was acquired
60 1–7 years ($\mu = 2.35$, $\sigma = 0.71$ years) after the first acquisition. Further details regarding recruitment protocols are provided
61 elsewhere¹⁴. Imaging sessions that did not pass the existing UKB preprocessing and quality control pipeline⁸ were excluded.

62 MRI data acquisition and existing preprocessing

63 A detailed description of the MRI data acquisition and preprocessing pipeline is provided elsewhere⁸. All modalities were
64 acquired on 3T Siemens Skyra scanners using the standard Siemens 32-channel head coil. The T1-weighted structural brain
65 images (Data-Field 20252) were acquired using a 3D MPRAGE acquisition at 1mm isotropic resolution with a 256mm
66 superior-inferior field of view⁸. The preprocessing steps included gradient distortion correction (GDC)^{16,17}, skull stripping¹⁸,
67 linear and nonlinear registration to MNI152 standard space^{19–21}, and defacing⁸. Additional derivative data precalculated and
68 provided by the UKB resource include macroscopic tissue segmentation with FSL FAST²², subcortical modeling with FSL
69 FIRST²³, and brain segmentation including cortical surface estimation with Freesurfer²⁴.

70 Resting-state BOLD data (Data-Field 25751) were acquired with a multi-band gradient echo EPI sequence^{25–27}, with an
71 acquisition time of ~6 minutes, for a total of 490 volumes, with a spatial resolution of 2.4mm isotropic voxels (TE/TR=39/735
72 ms, MB=8, no in-plane acceleration, flip angle 52°, conventional fat saturation)¹⁴. Preprocessing steps⁸ consisted of the FSL
73 MELODIC pipeline²⁸ (EPI susceptibility distortion correction, GDC, motion correction with FSL MCFLIRT²⁰, grand-mean
74 intensity normalization, and high-pass temporal filtering) followed by an ICA + FIX step to suppress remaining artifact
75 components^{29,30}.

76 Diffusion-weighted MRI (dMRI) data (Data-Field 20250) were acquired using a multi-band spin echo EPI sequence³¹,
77 with an acquisition time of ~7 minutes, with 100 unique diffusion sensitisation directions distributed equally across two shells
78 (b -values: 1000, 2000 s/mm^2), and 5 $b=0$ volumes, with a spatial resolution of 2mm isotropic voxels (MB=3, no in-plane
79 acceleration, TE/TR=92/3600 ms, partial Fourier 6/8, conventional fat saturation). 3 additional $b=0$ volumes were acquired
80 with reversed phase encoding direction to enable susceptibility field estimation³². The data were preprocessed with a pipeline⁸
81 consisting of correction for eddy current and head motion^{33–35} followed by GDC³⁶. Additionally, FSL's dtifit³⁷ and the
82 NODDI toolbox³⁸ were used to generate voxelwise microstructural parameters: fractional anisotropy (FA), tensor mode (MO),
83 mean diffusivity (MD), $b=0$ signal intensity (S0), intra-cellular volume fraction (ICVF), isotropic volume fraction (ISOVF),
84 and orientation dispersion index (ODI).

85 Connectomic nomenclature

86 Table 1 provides brief definitions for terms commonly used in this paper.

Term	Definition
Template space	A surface-based (e.g. FreeSurfer's "fsnative" and HCP's "fs-LR"), or volumetric (e.g. MNI 152) common brain space that is normally used for group-level neuroimaging studies ³⁹ .
Native space	The space in which a subject's brain imaging data is originally provided.
Registration	Computing a transformation that best aligns a subject's native space MRI data to a template space.
Brain atlas	A standard map of regional delineations segmenting the cortical and subcortical gray matter into discrete brain regions. These maps are conventionally provided in a standard template space.
Atlas parcellation	The transformation of a brain atlas from template space to subject's native space provides a parcellation map delineating different brain regions in an individual.
Brain network / Connectome	A measure of inter-regional structural or functional relationships stored in the form of a two-dimensional connectivity matrix ⁴⁰ . Rows/columns of this matrix quantify inter-regional connectivity properties from a region of interest (ROI) in the gray matter. Atlas parcellations can be used to define ROIs.
Tractography	A computational method to estimate anatomical trajectories of white matter fiber pathways from dMRI data ⁴¹ .
Streamline	A set of 3D coordinates encoding trajectory estimates yielded from tractography.
Structural connectome	A connectome constructed from tractography results in which edges quantify properties describing anatomical connections between ROIs (e.g. number of streamlines, or connection length) ⁴² .
Functional connectome	A connectome constructed from fMRI data in which edges quantify pairwise functional associations between multivariate time-series describing the regional blood-oxygen-level-dependent (BOLD) signal sampled from ROIs ⁴³ .

Table 1. A description of frequently used terms.

87 Connectome reconstruction pipelines

88 As detailed below, we developed novel connectome reconstruction pipelines to satisfy five competing demands:

- 89 90** *1. Connectome quality*, producing high-quality brain networks by using state-of-the-art pipelines to infer interregional brain connectivity from diffusion and functional neuroimaging data.
- 91** *2. Accessibility*, facilitating streamlined access to connectome data in an efficient and easy to use format.
- 92** *3. Flexibility*, enabling users to choose from connectomes mapped using a broad range of methodological preferences.
- 93 94** *4. Computational requirements*, as our pipeline needed to be executed on data from ~45,000 MRI sessions, which is a considerable burden even when making use of high-performance computing (HPC) services.
- 95 96** *5. Storage requirements*, as the generated connectivity data needs to be stored both in the short term on local storage during calculation, and in the long term on UKB storage infrastructure.

97 Hence, the pipeline was developed to provide a good balance between these competing aims and prepare a comprehensive, **98** versatile, and high-quality brain connectivity resource. This included the development of new utilities in software packages **99** used to map connectomes (e.g., *MRtrix3*⁴⁴) with an explicit focus on reducing computational and storage requirements.

100 A crucial conflict identified within this set of demands lies at the intersection of accessibility, flexibility, and storage **101** requirements. On the one hand, user flexibility is boosted by providing many versions of the same connectome, mapped **102** according to different methodological choices, such as different atlases or interregional connectivity measures. On the other **103** hand, catering for flexibility leads to a combinatorial increase in the number of connectomes, which would be prohibitively

104 expensive to store and access for all UKB subjects. This would be particularly the case for SC matrices, for which there are
105 many options for the metric of connectivity.

106 We addressed this important issue as follows. For a subset of connectome configurations, deemed to be of broad applicability,
107 connectivity matrices were calculated and uploaded to the UKB for direct user access. Where an alternative configuration
108 is desired, we provide both the requisite intermediate data (ie. for which the most expensive computational processes have
109 already been performed) and a software tool that uses these data to efficiently calculate the connectome of interest, such that
110 any combination of connectome attributes can be chosen. This tool, along with the relevant code for the pipeline in its entirety,
111 is accessible from github.com/sina-mansour/UKB-connectomics.

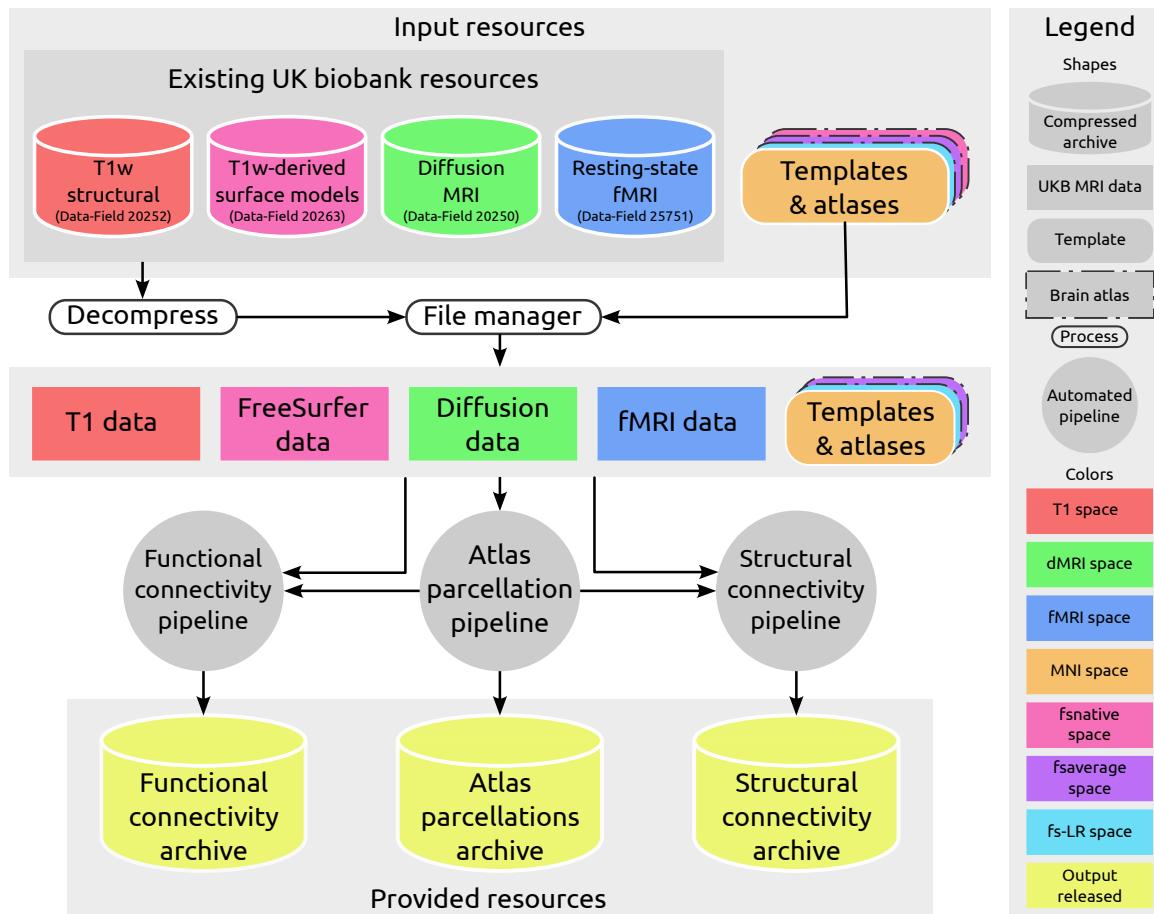


Figure 2. Schematic flowchart of the complete pipeline. Compressed bulk data archives from UKB along with publicly available brain parcellation atlases and templates were used as inputs of the connectivity mapping pipelines. These inputs were used in three separate steps to generate parcellations in subject space, that were subsequently utilized in functional and structural connectome construction pipelines. Flowcharts of these steps are detailed in the ensuing figures. For every imaging session, the outputs of these three steps are provided as separate compressed archives.

112 An overview flowchart of the pipeline is presented in Figure 2. In short, a set of automated pipelines were implemented to
113 perform three main tasks:

- 114 1. *Atlas parcellations*: Generate volumetric atlas parcellations in subject space, segmenting cortical and subcortical gray
115 matter into distinct brain regions
- 116 2. *Functional connectivity*: Derive resting-state functional time series of brain activity within these parcels to enable
117 functional connectivity (FC) estimation
- 118 3. *Structural connectivity*: Estimate white matter fiber orientations from diffusion MRI data and perform tractography to
119 map structural connectivity (SC) matrices

120 The following sections provide a detailed explanation of every step in the connectome reconstruction pipeline.

121 **Brain atlas parcellations**

122 For parcellation of the cortical and subcortical gray matter into distinct nodes of a connected network, here we focus strictly
 123 on the conventional approach in the domain of neuroimaging connectomics, where spatial correspondence is established
 124 between a pre-generated atlas defined in some template space and the subject-specific T1-weighted image (see Table 1)^{40,42}.
 125 Importantly, it is well established that the choice of atlas, and in particular the granularity of gray matter segmentations, may
 126 impact findings in brain connectivity studies^{45,46}. To address this issue, as shown in Figure 3, we consider a total of 23 cortical
 127 and 4 subcortical atlases. This provides researchers with the ability to choose the most appropriate parcellation for their study,
 128 investigate connectivity features at multiple spatial scales, and replicate analyses across different parcellation schemes.

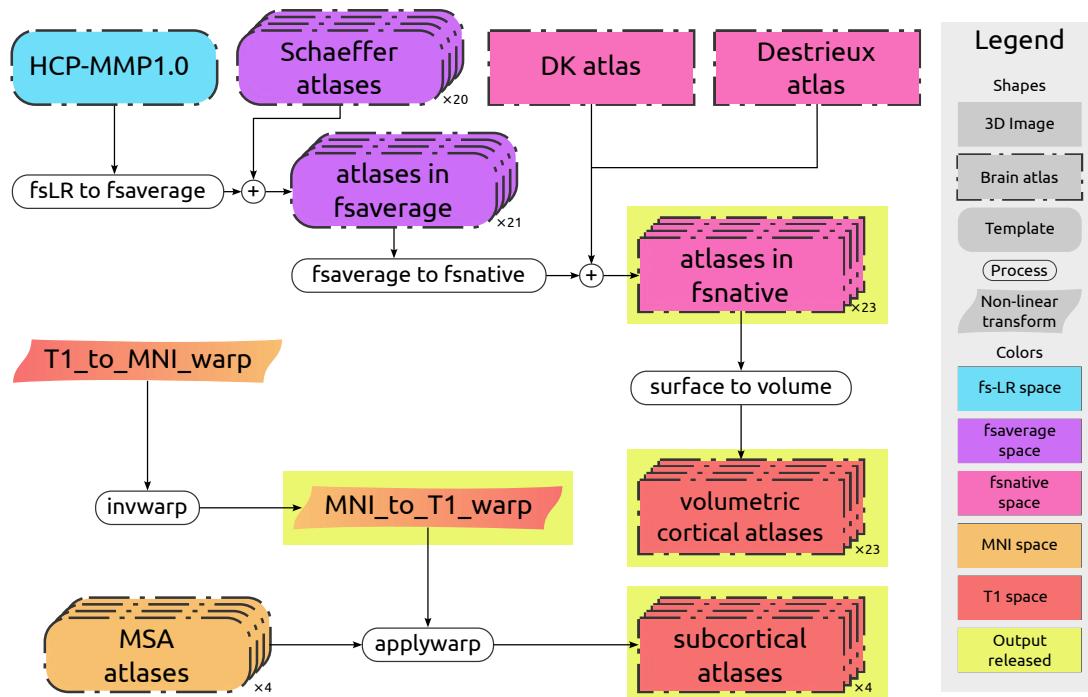


Figure 3. Flowchart for the brain atlas parcellation pipeline. A total of 23 cortical and 4 subcortical atlases, transformed from their respective template spaces, were mapped to each individual's native volumetric space. These volumetric atlas parcellations, as well as additional supporting files (volumetric warp and native surface delineations of cortical atlases), are made available in the atlas parcellations compressed archive (indicated with yellow highlight).

129 An important detail of our handling of parcellation data is that cortical and subcortical gray matter parcellations were
 130 processed entirely independently of one another, and are only combined immediately prior to connectome construction. This
 131 permits independent selection of both cortical and subcortical parcellations for any given connectome configuration.

132 We computed volumetric brain atlases in every individual's native space for a total of 23 cortical and 4 subcortical
 133 atlases of the human brain. The cortical atlases included 20 different Scheaffer parcellations⁴⁷ (derived from two different
 134 sets of functional networks⁴⁸ and sub-divided into different parcellation granularities ranging 100–1000 nodes), the Human
 135 Connectome Project's multimodal parcellation⁴⁹ (HCP-MMP1.0; also known as the Glasser atlas), the Desikan-Killiany atlas⁵⁰
 136 (FreeSurfer's "aparc"), and the Destrieux Atlas⁵¹ (FreeSurfer's "aparc.a2009s"). The subcortical atlases included 4
 137 different spatial scales of the Melbourne Subcortical Atlas (MSA)⁵².

138 All atlases were transformed to each individual's native volumetric space. For the subcortical atlases, the UKB provides
 139 non-linear warp files from the subject's T1-weighted image to the MNI152 template²¹, which is the space in which the MSA
 140 parcellations are defined. We first computed the inverse of this warp (ie. from MNI152 to the subject's T1-weighted image),
 141 then applied this transformation to each of the four parcellations using nearest-neighbor interpolation (FSL's "applywarp").
 142 To map subject-specific cortical atlases, we started from surface-based labels provided in different template spaces^{47,49–51}. For
 143 each participant, we aligned these labels to the subject's native cortical surface representation (FreeSurfer's "fsnative"),

as this provides superior anatomical accuracy compared to volumetric registrations. To transform surface labels into the final volumetric atlases, we first defined, for each subject, a cortical ribbon at the interface between gray and white matter. Lastly, we assigned every voxel in the ribbon the label of its nearest surface vertex. The surface transformations made use of in-house methods incorporating various functionalities from the Connectome Workbench⁵³, FreeSurfer²⁴, and NiBabel⁵⁴. All parcellations in subject space (both surface and volumetric representations), the inverse nonlinear MNI warp, and associated conversion scripts (to expedite use of atlases not processed here) are made available (see *Data Records and Code Availability*).

Additional scripts are also provided to combine cortical and subcortical atlases, which are required for mapping SC matrices comprising combinations of cortical and subcortical parcellations beyond the ones readily provided in our resource (see *Structural connectivity: matrices* section for detail).

In some circumstances, both cortical and subcortical sources may attribute a parcel to the same voxel in native space. This occurred most predominantly in the hippocampal region when using the HCP-MMP 1.0 / Glasser atlas. The software used for connectome construction and provided to the research community prioritizes cortical labels where this occurs.

Functional connectivity

FC characterizes statistical dependencies between the BOLD time series recorded from different brain regions⁴⁰. Several computational approaches can be used to map functional connectivity from BOLD signals^{4,55}. Here, we provide regionally averaged BOLD time series for the same brain parcellations atlases used to map SC matrices. This enables researchers to easily compute FC matrices using their favorite methods, and also allows for analyses of dynamic and time-varying FC. The flowchart of FC processing is shown in Figure 4. All parcellations were first resampled from the subject's T1-weighted image voxel grid to the subject's preprocessed fMRI voxel grid (FreeSurfer's `mri_vol2vol`). For each parcel, the mean time series across the fMRI voxels ascribed to that region was calculated. By providing these parcellated BOLD time series, we enable flexibility and convenience in mapping functional connectivity across a wide range of alternative spatial resolutions and methodological approaches. For instance, FC derived from statistical correlation-based measures (e.g. Pearson's r) can be directly computed from the time series data in a few milliseconds.

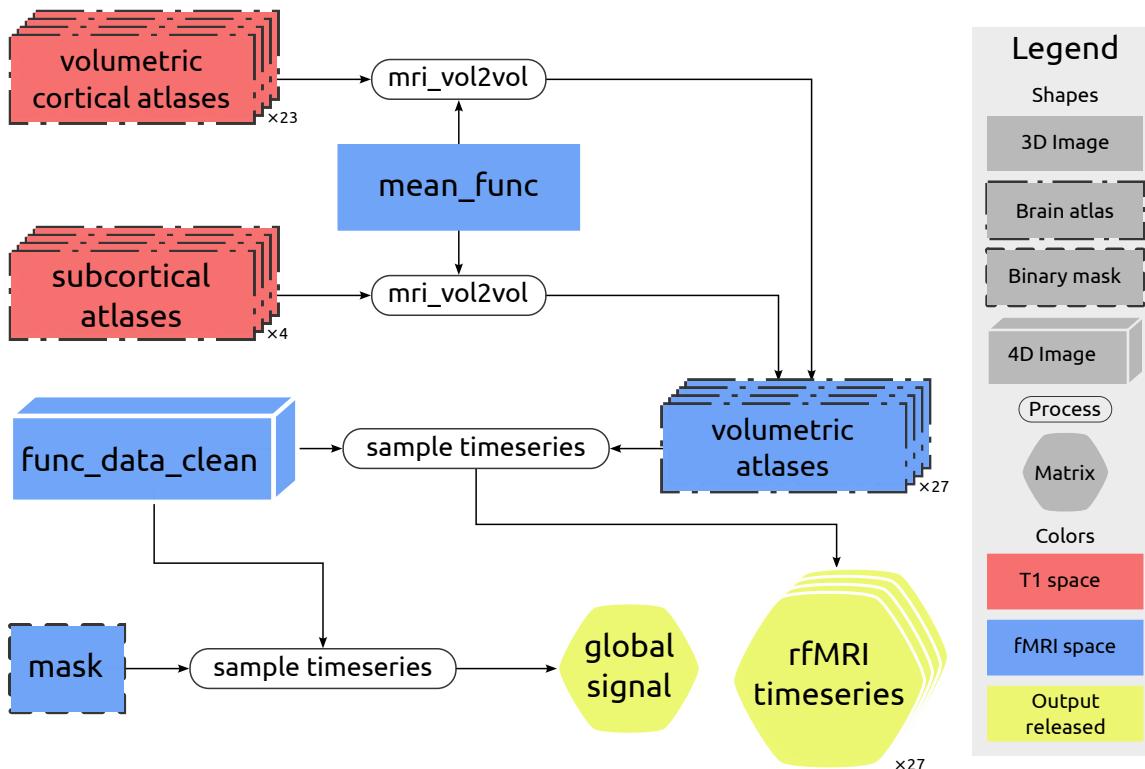


Figure 4. Flowchart for the functional connectivity mapping pipeline. BOLD regional time series are provided for 27 brain parcellation atlases, enabling rapid computation of functional connectivity matrices. The global signal time series was additionally computed. Note: yellow color indicates output resources that are made available in the functional connectivity compressed archive.

167 Global signal regression (GSR) is an fMRI preprocessing technique with potential merits and drawbacks that are subject
 168 to debate^{56–64}. We thus calculated the global signal time series and provide those data separately to provide researchers with
 169 the flexibility to perform GSR if desired. The global signal was computed by averaging the BOLD time series over all voxels
 170 belonging to the anatomical brain mask.

171 **Structural connectivity: tractography**

172 Structural connectomes provide a network representation of the brain white matter axonal architecture⁴⁰. Whole-brain
 173 tractography is used to map white matter axonal pathways from an individual's diffusion MRI data and enable estimation of
 174 the connectivity properties of these pathways using any of a number of structural connectivity measures. Figure 5 shows how
 175 whole-brain tractograms were computed using probabilistic tractography as implemented in *MRtrix3*⁴⁴.

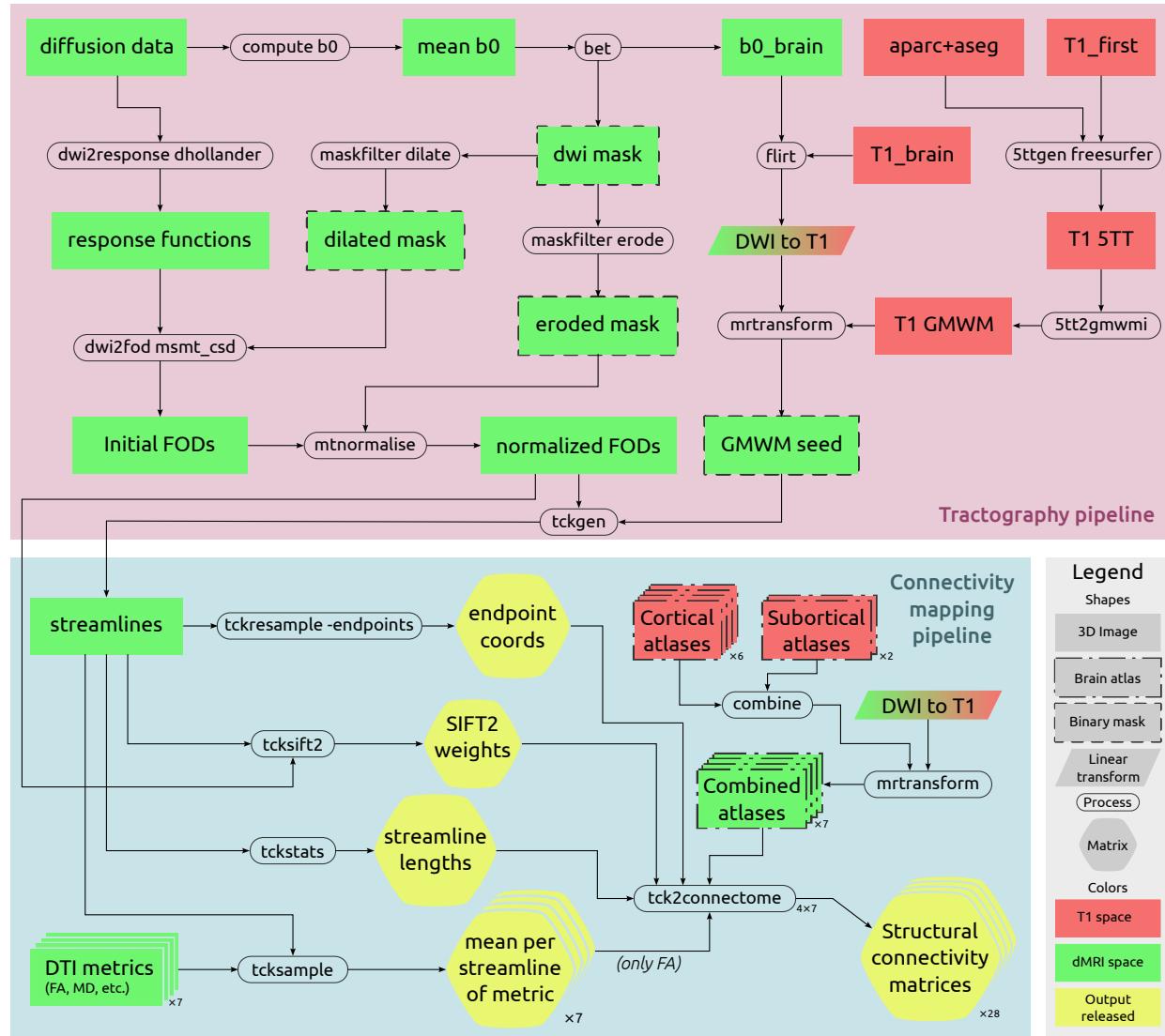


Figure 5. Flowchart for the structural connectivity mapping pipeline. The pipeline is divided into two sections. First, white matter tractography is used to generate streamlines from diffusion-weighted imaging data. Next, these streamlines are used to estimate interregional connectivity properties based on various measures of structural connectivity. The streamline endpoint coordinates, connectivity metrics per streamline, and the subset of 28 connectome matrix configurations that were explicitly generated, are all provided in the structural connectivity compressed archive (shown in yellow).

176 A brain mask was derived by skull-stripping the mean of DWI volumes without any diffusion weighting ($b=0$ volumes)
 177 and executing the FSL bet tool with parameters tuned for diffusion-weighted imaging (DWI) data¹⁸. In comparison to the
 178 DWI masks provided by the UKB, these masks were deemed more accurate and resulted in better registration between the

179 T1 and DWI spaces. Macroscopic tissue response functions⁶⁵ for white matter (WM), gray matter (GM), and cerebrospinal
180 fluid (CSF) were estimated with an unsupervised heuristic^{66,67}. Multi-shell, multi-tissue (MSMT) constrained spherical
181 deconvolution (CSD)⁶⁸ was used to estimate fiber orientation distributions (FODs). This multi-tissue information was used
182 to perform combined intensity normalization and bias field correction⁶⁹. Liberal and conservative brain masks were used
183 respectively for these two steps to mitigate the detrimental influences of imperfect masks in the respective processes.

184 Whole-brain tractography was performed as follows. A tissue-type segmentation image, intended for use of the Anatomically-
185 Constrained Tractography (ACT) framework⁷⁰, was constructed using a combination of the FreeSurfer `aseg` image and the
186 results of FSL FIRST²³. From this, a mask of the interface between GM and WM was constructed for the purpose of streamline
187 seeding. Probabilistic tractography was performed using 2nd-order integration over Fibre Orientation Distributions (iFOD2)⁷¹.
188 A total of ten million streamline seeds were drawn throughout the GM-WM interface, and generated streamlines were rejected
189 if they failed to satisfy length constraints or the ACT priors⁷⁰. This constant number of streamline seeds is an important
190 requirement for computational tractability that provides a more robust upper bound on execution time across sessions.

191 **Structural connectivity: matrices**

192 Tractography streamlines and parcellation images were next used to generate SC matrices quantifying various connectivity
193 measures for each regional pair. To generate structural connectomes that are representative of whole-brain connectivity, we used
194 parcellations that integrated both cortical and sub-cortical atlases. As described previously, structural connectivity matrices were
195 pre-calculated for only a subset of all possible connectome configurations; the seven combinations of cortical and subcortical
196 parcellations chosen—for which pre-computed out-of-the-box connectivity matrices are available—are summarized in Table 2.
197 Nevertheless, the provided scripts and supplementary data (e.g. streamline endpoint coordinates and per-streamline metrics)
198 enable connectivity reconstruction for any other possible combination of cortical and subcortical parcellation schemes desired.

Cortical atlas	Cortical regions	Subcortical atlas	Subcortical regions	Total regions
Desikan Killiany	68	MSA - scale I	16	84
Destrieux	148	MSA - scale I	16	164
Glasser	360	MSA - scale I	16	376
Glasser	360	MSA - scale IV	54	414
Schaeffer 200 (7 networks)	200	MSA - scale I	16	216
Schaeffer 500 (7 networks)	500	MSA - scale IV	54	554
Schaeffer 1000 (7 networks)	1000	MSA - scale IV	54	1054

Table 2. The seven combinations of cortical and subcortical parcellations for which structural connectivity matrices were precomputed, and their respective numbers of regions.

199 Numerous measures of structural connectivity strength are available. The most common measure is the streamline count,
200 which quantifies the total number of streamlines connecting region pairs. Alternatively, post processing algorithms can be
201 applied to ensure that streamline counts better reflect the underlying white matter architecture. We provided per-streamline
202 "weights" calculated by the SIFT2 method to estimate the Fiber Bundle Capacity (FBC) between regions⁷². Additionally, the
203 average length of all streamlines between region pairs were computed to measure connection length. Finally, microstructural
204 parameters (i.e. FA, MD, MO, S0, ICVF, ISOVF, and ODI) were averaged for each streamline trajectory to quantify the
205 microstructural properties of connections.

206 Regarding the subset of connectome configurations for which we provide pre-computed structural connectivity matrices, for
207 each of the combined parcellation schemes as shown in Table 2, matrices were constructed utilizing the following four metrics:

208

- Streamline count
- Fiber Bundle Capacity (from SIFT2)
- Mean streamline length
- Mean Fractional Anisotropy (FA)

212 For *all* structural connectivity metrics (ie. not only those for which matrices were pre-computed), the per-streamline
213 quantitative metrics are provided alongside the locations of the endpoints of streamlines. This facilitates the construction of

214 structural connectomes using any preferred combination of cortical parcellation, subcortical parcellation, and connectivity
215 metric, utilizing the provided connectome generation scripts; this requires both minimal storage (only a pair of 3-vectors and a
216 single floating-point value per streamline) and minimal additional computation (as it is the propagation of streamlines that
217 incurs the greatest expense; assigning streamline endpoints to a parcellation is comparably simple). Considering all different
218 parcellations and connectivity metrics, our code and data resources allow for user-friendly and time-efficient reconstruction of
219 ~ 1000 alternate structural connectivity matrices for a single subject. We further note that the data provided in this form are
220 entirely compatible with the adoption of recent developments in the domain such as high-resolution connectomes that consider
221 each surface vertex as its own parcel⁷³, and the utilization of spatial smoothing of parcels to enhance reliability⁷⁴, for which the
222 relevant software tools are also provided.

223 Computing resources

224 The whole pipeline was tailored for parallel execution on high-performance computing (HPC) clusters. Parallelization was
225 implemented at the level of individual imaging sessions, with a separate computation job submitted for every session ($\sim 45,000$
226 parallel job submissions). While many of the underlying software tools are capable of executing multiple threads for a single
227 processing job, this was not the case for *all* such tools, and therefore allocating a single CPU core per session was determined
228 to yield the best CPU resource utilization. The maximal memory and wall time per job were empirically minimized to facilitate
229 maximal parallelization on the HPC resource without compromising completion of jobs; this was chosen to be 4GB RAM and
230 6 hours execution time. The Spartan HPC resource provided by the University of Melbourne^{75,76} was utilized for this task,
231 which was typically capable of executing 100–200 such jobs in parallel depending on external utilization.

232 Time requirements

233 In addition to the three primary computation steps of the pipeline, each computing job also involved downloading all required
234 UKB data and uploading the resulting derivatives. While data download would typically only require minutes, UKB servers
235 permit only 10 parallel downloads per user, and some jobs could hence experience considerable delays in accessing their
236 requisite data; the wall time allocated for each job was therefore set in order to tolerate such delays without resulting in job
237 failure.

238 Following data download, the approximate processing time required for each stage of the pipeline was as follows. The atlas
239 mapping pipeline required 10 minutes. Mapping resting functional data required 5 minutes. The most time-consuming step was
240 the structural connectivity reconstruction pipeline, which required 150 minutes. Finally, subsequent conversions and upload
241 steps required 5 minutes. Overall, the complete pipeline required 3–4 hours to finish for a single imaging session.

242 In total, mapping connectomes across all UKB imaging sessions required $\sim 200,000$ CPU hours (~ 20 years) of computation
243 to complete. This substantial time requirement could only be satisfied with the extensive use of HPC resources in parallel
244 execution which reduced the overall required time to map these connectomes from years to months⁷⁵.

245 Storage requirements

246 The storage requirements for the derivatives of the analysis pipelines are as follows:

- 247 • *Atlas parcellation pipeline*: Cortical and subcortical parcellations warped to native subject space, in addition to the
248 non-linear warp from MNI to subject space (to facilitate researcher utilisation of other parcellations represented in
249 MNI152 space), all stored in NIfTI format in a compressed archive, requires ~ 100 MB per session.
- 250 • *Functional connectivity pipeline*: The 28 time series (each unique cortical and subcortical parcellation as well as the
251 global signal, as detailed in previous sections) are provided in comma-separated values (CSV) format. These files are
252 provided as a compressed archive with a size of ~ 50 MB per session.
- 253 • *Structural connectivity pipeline*: The combination of parcellations, pre-calculated structural connectome matrices, stream-
254 line endpoint coordinates, and per-streamline quantitative metrics for construction of other connectome configurations,
255 are provided as a compressed archive with a size of ~ 75 MB per session.

256 As a result, a total of ~ 225 MB of storage is required to store all derived data per session. The complete set of computed
257 connectivity maps across all sessions occupies ~ 10 TB of storage.

258 Data Records

259 The generated files are organized into three separate compressed archives for every UKB imaging session. Figure 6 provides a
260 summarized list of files provided for a single session. Supplementary Figure S1 provides a more detailed list of all files. All
261 data are made available via UKB data returns policy and will be accessible as new bulk files.

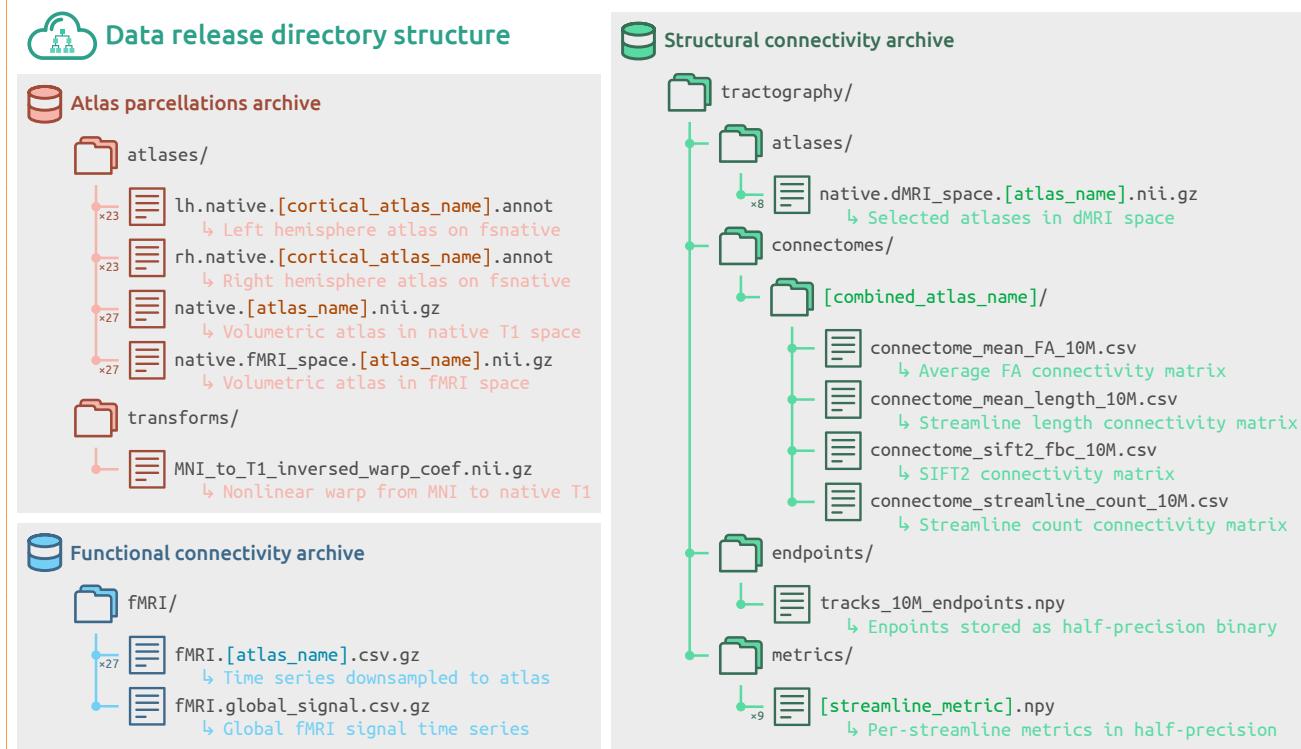


Figure 6. Summary of file archives comprising the connectome resource. Three separate compressed archives are provided for atlas parcellations (red), functional time series (blue), and structural connectivity data (green). Alternative configurations of provided data are summarized by providing a single informative placeholder (colored text in square brackets). A detailed list of all files is provided in Supplementary Information.

262 **Atlas data**

263 The compressed bulk file of atlas data contains derivative parcellations in native volumetric space (atlases/native. 264 [atlas_name].nii.gz) for all cortical and subcortical atlases used. Cortical atlases are also provided as parcel- 265 lated surface data in the FreeSurfer "fsnative" space (atlases/(rh|lh).native.[atlas_name].annot). The 266 warp image that can be used for nonlinear transformation from MNI space to native coordinates is additionally provided 267 (transforms/MNI_to_T1_inversed_warp_coef.nii.gz).

268 **Functional data**

269 The compressed bulk file of functional data contains time series aggregated within the parcels of various atlases. The time 270 series information is stored as a compressed file with comma-separated values, i.e. the .csv.gz format. For each atlas, all 271 sampled time series are provided in a single bulk file (fMRI/fMRI.[atlas_name].csv.gz). In addition, the time series 272 for the global signal is included (fMRI/fMRI.global_signal.csv.gz).

273 **Diffusion tractography data**

274 The compressed bulk file of diffusion data contains:

- 275 • 28 pre-calculated connectivity matrices (all combinations of the combined atlases shown in Table 2 and the four 276 primary connectivity metrics listed in the "Structural connectivity: matrices" section), with paths: (tractography/ 277 connectomes/[cortical_atlas_name]+[subcortical_atlas_name]/connectome_[metric_name]_10M.csv).
- 278
- 279 • Spatial locations of all streamline endpoints: (tractography/endpoints/tracks_10M_endpoints.npy). This 280 facilitates assignment of pre-generated streamlines to any parcellation of interest. This file is stored in a half-precision 281 floating-point format (16 bits) to reduce storage requirements with minimal loss of precision.
- 282
- 283 • Nine per-streamline quantitative metrics, with paths: tractography/metrics/[metric_name].npy. Metrics include streamline length, SIFT2 weights, and mean values of voxel-wise quantitative metrics along the streamline

284 trajectories. These are also stored in half-precision floating-point format, with multiplicative factors of $1e^3$ and $1e-3$
 285 applied to the mean MD and mean S0 metrics, respectively, to scale the magnitudes of floating-point values toward unity
 286 and therefore mitigate loss of precision.

287 • Statistics regarding tractogram generation (eg. why streamlines were terminated and why they were accepted or rejected).
 288 • Statistics regarding the operation of the SIFT2 algorithm.

289 Data Validation

290 All brain imaging data sourced as inputs passed the automated quality control (QC) evaluations by UKB⁸. We additionally
 291 computed various assurance metrics to assess the quality of the provided connectomic resource. These evaluations can be
 292 divided into i) QC metrics to probe data quality and ii) analyses of topological properties of brain networks, showing that our
 293 connectomes reproduce established findings of the network neuroscience literature.

294 Quality control

295 We have computed an extensive set of connectomic QC measures. These metrics complement existing QC efforts provided by
 296 the UKB, and can be used to exclude low-quality or inaccurate connectomes. Figure 7 provides a summary of the provided QC
 297 measures.

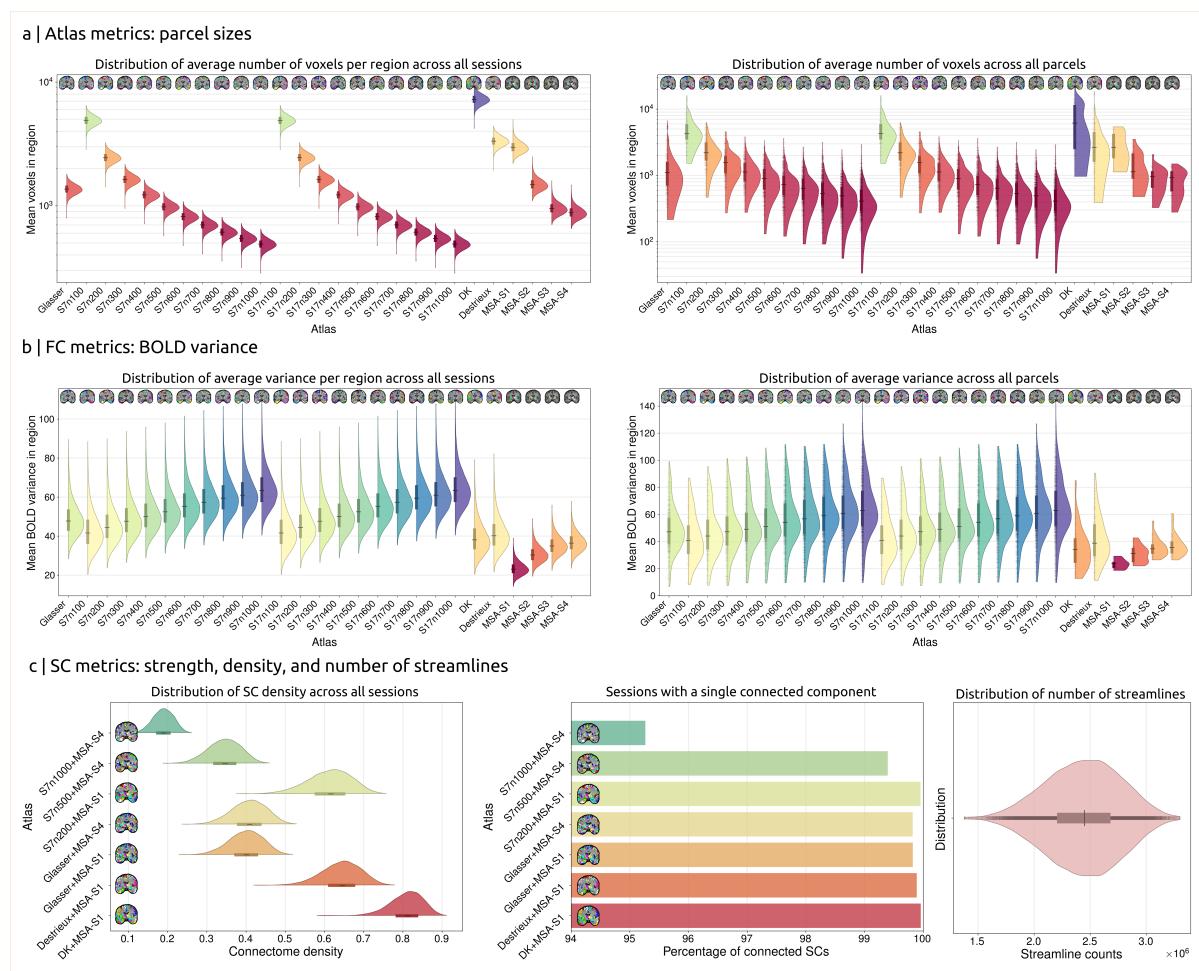


Figure 7. Quality control measures. (a) For atlas parcellations, the parcel sizes were quantified by the number of voxels within each region. Distributions of the number of voxels averaged across atlas regions (left) and across imaging sessions (right) summarize the trends in parcel size for all 27 cortical and subcortical atlases. (b) Similarly, distribution of BOLD signal variance is shown for all 27 atlases. (c) Summary of structural connectivity QC measures for connectome density, components, and reconstructed streamlines for all sessions.

298 Our QC measures serve as basic features that can be utilized to generate flexible data exclusion criteria tailored to specific
299 research questions. For instance, cases where such metrics lie at the tail of the corresponding distribution could be excluded from
300 analysis, or QC features could be matched between groups. We suggest that these QC features should be tailored to particular
301 study aims, rather than being adopted blindly. For instance, one study may use the metric of total number of streamlines in
302 the connectome to exclude individuals where tractography reconstruction is poor, or account for this effect as a confounding
303 covariate; in contrast, another study aiming to assess the impact of a particular pathology on the structural integrity of the
304 connectome may consider the total number of streamlines to be a variable of interest that should *not* be matched/regressed.

305 **Atlas QC measures**

306 For all volumetric parcellations (cortical and subcortical), the volume of every atlas region in an individual was computed
307 as the total number of voxels assigned to each region. This measure can be used to investigate properties of the native atlas
308 parcellations. Future studies may decide to exclude sessions or parcellations for which certain regions are not appropriately
309 represented, e.g. if a region has no (or very few) voxels. In addition, these measures can optionally be used for normalization of
310 particular structural connectivity matrices: since larger brain regions are more likely to be intersected by streamlines, one may
311 choose to rescale connectivity based on regional volume^{2,77}.

312 Figure 7.a shows a summary of this QC measure in the UKB sample. Violin plots on the left depict the distribution of
313 voxel sizes averaged across all regions and plotted across sessions. Conversely, the plot on the right is averaged across sessions
314 and depicts the distribution across regions. As anticipated, parcel volumes tend to become smaller as the granularity of the
315 parcellation scheme increases. Furthermore, it indicates that a considerable degree of size variation exists between different
316 regions of the same atlas; for instance, the largest regions of Schaeffer's atlas with 1000 parcels are similar in size to regions
317 from the Destrieux atlas with only 148 parcels.

318 **Functional connectivity QC measures**

319 For functional time series, the variance of the aggregated signal within each region is reported across all sessions and atlas
320 regions. This regional measure of variance can be compared to the variance of the global signal to provide an estimate of
321 signal quality⁷⁸. However, it is important to interpret this information with caution, as the standard deviation of an fMRI signal
322 cannot be equated to noise strength and is known to vary with aging and cognition^{79,80}. Signal variance could still be used as a
323 quantitative quality metric to filter out low quality scans.

324 Figure 7.b provides summary distribution plots of signal variance averaged across sessions and parcels. These summary
325 plots show that relatively higher granularities (e.g. 1000 cortical regions compared to 100 cortical regions) tend to contain
326 signals with larger variation. This is because large parcels sample fMRI over more voxels, which eliminates variance sources
327 from localized effects and unstructured noise. These variance measures for QC could potentially be used as exclusion criteria
328 for sessions in which a region has zero (or very low) variance. A retrospective evaluation of this QC measure indicated a
329 limitation in UKB fMRI preprocessing pipelines impacting signal quality at the orbitofrontal cortex, which is known to be
330 susceptible to BOLD signal loss^{81,82} (see Supplementary Information for further detail).

331 **Structural connectivity QC measures**

332 For structural connectivity, the number of streamlines reconstructed by tractography is reported as a measure of whole-brain
333 tractogram reconstruction efficacy. Given that the number of seeded streamlines is constant for all individuals (10 million),
334 a lower total streamline count indicates higher exclusion rates from streamline acceptance criteria (anatomical validity as
335 determined by ACT and adequate length), which may indicate pathology, poor structural integrity, or low quality data. Another
336 use of this feature is normalizing the connectivity matrices to construct connectomes with equal total strength, which can be
337 more suitable for studying connection probability⁸³. In addition, the number of connected components and total connectome
338 density were computed for every structural connectivity matrix. This provides an additional QC feature, as connectomes are
339 expected to form a single connected component and therefore disconnected connectomes could indicate either gross structural
340 abnormalities or poorly reconstructed structural connectivity. Hence, future studies could exclude SC matrices with more than
341 one connected component. As shown in Figure 7.c, SC forms a single connected component for most of the sessions (> 95%
342 for the highest granularity, and > 99% for other granularities). Finally, the weighted nodal strength and binary nodal degree
343 are provided, with a binarization threshold of one streamline. Figure 7.c summarizes the QC metrics extracted for structural
344 connectomes.

345 **Properties of structural and functional connectomes**

346 In this last section, we provide an initial exploration of the properties of our structural and functional brain networks. The
347 following analyses sought to replicate previously established results in the network neuroscience literature and, as such, further
348 demonstrate the quality and utility of our connectivity resource.

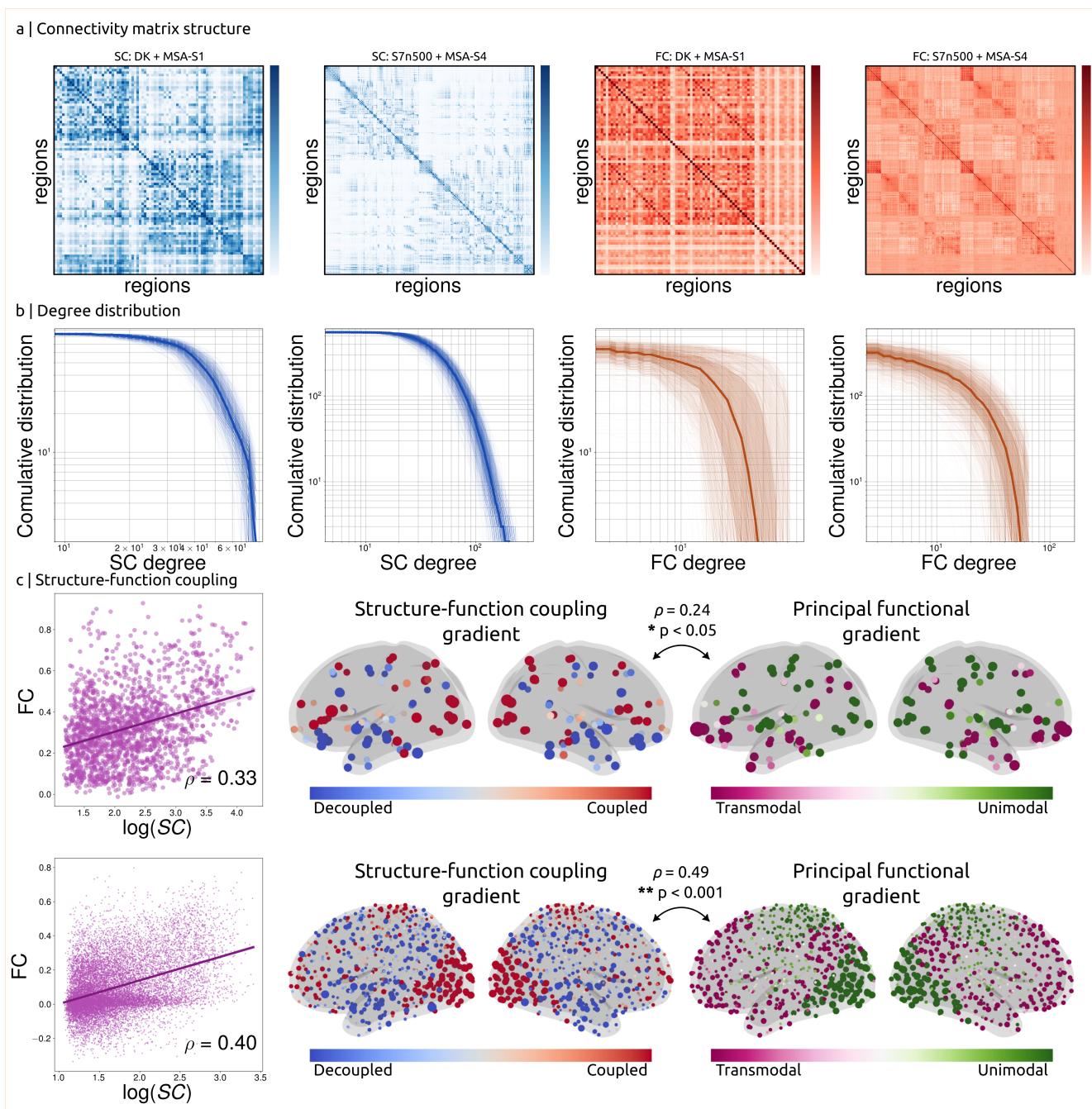


Figure 8. Properties of structural and functional brain networks. (a) Group-level connectomes were derived from 1000 random sessions. The matrices closely resemble standard brain connectivity characteristics with visual distinctions between the cortical hemispheres and the subcortex, local clusters of connectivity within each hemisphere, and strong homotopic connections forming diagonal strides. Results are presented for both SC (blue) and FC (red) matrices in two exemplar parcellations, with "DK + MSA-S1" containing the fewest and "S7n500 + MSA-S4" containing one of the greatest numbers of nodes. (b) Degree distributions of individual connectomes used to construct the group-level matrices. Thin lines indicate trajectories for individual session data; thick line presents the median; shaded regions indicate [25, 75] and [5, 95] centiles. (c) Structure-function coupling was quantified for both exemplar parcellations. Brain-wide coupling was assessed using Pearson's correlation between FC and $\log(\text{SC})$ across all edges (scatter plots). Node-wise coupling gradients were computed to project regions to a spectrum of decoupled (blue) to coupled (red) areas. These gradients were compared with FC-derived gradients of functional hierarchy in which regions are situated on a gradient from unimodal (green) to transmodal (purple) areas.

349 To this end, group-level structural and functional networks were constructed from connectivity data of 1000 randomly
350 sampled individuals. We considered two parcellation combinations comprising a total of 68 (cortex: DK, subcortex: MSA-S1)
351 and 554 (cortex: Schaefer 500, subcortex: MSA-S4) gray matter regions. FC was mapped using GSR and the pairwise Pearson
352 correlation of regional BOLD signals. Group-level FC was computed as the average of functional networks across the 1000
353 subjects and group-consensus SC was inferred using consistency-based thresholding⁸⁴.

354 Figure 8.a shows the resulting group average SC (blue) and FC (red) matrices for the two selected parcellation schemes.
355 These visualizations align with previous literature^{2,85,86} and exhibit features that are consistent with typical connectomes,
356 including i) distinct inter-hemispheric and cortico-subcortical boundaries, ii) a modular structure evident within each hemisphere,
357 and iii) evidence of homotopic connections between the two hemispheres.

358 Next, we assessed the scale-free network property of the connectomes. We computed the degree distribution of the FC
359 and SC matrices for all sessions by assuming respective binarization thresholds of $\rho = 0.4$ and 1 streamline, respectively. The
360 degree distributions of the resulting matrices are presented in Figure 8.b. The corresponding degree distribution plots replicate
361 previous findings of characteristics observed in structural and functional connectomes with a degree distribution that follows an
362 exponentially truncated power law⁸⁶⁻⁹¹.

363 Finally, we sought to reproduce previous findings of SC-FC coupling (Figure 8.c). The structure and function of the
364 human brain networks are interrelated^{92,93}. This relationship can be investigated by comparing the strengths of structural and
365 functional network edges. We present data for three experiments in this regard:

- 366 1. *Structure-function correlation*: We assessed the degree of collinearity between FC strengths and the logarithm of SC
367 strength (as quantified by streamline count). The expected positive correlation^{94,95} between the strength of structural and
368 functional connectivity was observed for atlases with high ($\rho = 0.4$) and low ($\rho = 0.33$) parcellation granularities.
- 369 2. *Structure-function coupling gradient*: The degree of structure-function coupling is reported to vary across the brain,
370 with certain regions exhibiting stronger coupling and others displaying relatively decoupled activity⁹⁶⁻⁹⁹. To evaluate
371 structure-function coupling at the level of individual regions, we used a multilinear prediction approach⁹⁶; in short,
372 for each node, we estimated the FC strength to all other nodes via multilinear regression based on four measures of
373 inter-regional distance and structural communication: (i) Euclidean distance, (ii) structural connectivity, (iii) shortest
374 path length, and (iv) communicability¹⁰⁰. The accuracy of model predictions (quantified by Pearson's correlation) is
375 indicative of local SC-FC coupling strength.
- 376 3. *Principal functional gradient*: In prior work, these local patterns of regional coupling have been reported to follow
377 the functional organization hierarchy of unimodal to transmodal brain regions^{97,98}. We thus computed the principal
378 functional gradients by performing diffusion map embedding on group-level FC¹⁰¹ and evaluated its association with the
379 SC-FC coupling gradient. Our results (Figure 8.c) successfully replicated the expected relationship between the coupling
380 patterns and functional organization hierarchy at low ($\rho = 0.24$) and high ($\rho = 0.49$) parcellation granularities.

381 The evaluations of network properties presented in this section demonstrate that the connectivity matrices provided here
382 reproduce well-established findings in brain connectivity research. This illustrates the high quality of this connectome resource
383 and its potential to facilitate future connectomic studies in an aging population.

384 Usage Notes

385 All data will be made available via UKB data returns policies to be accessible based on UKB material transfer agreements.
386 Researchers can apply to access these data by filling out a UKB access application. Additional code and data (such as the label
387 ordering of atlases) are made openly available in a publicly accessible git repository. All data are provided in formats that are
388 readable in various programming languages. This enables use of several existing software packages for brain connectivity
389 analysis such as the Brain Connectivity Toolbox (Matlab)¹⁰², bctpy (Python), and Nilearn (Python), as well as general network
390 analysis tools such as NetworkX¹⁰³.

391 Code availability

392 All scripts used to perform computations described in this manuscript (eg. generating atlas parcellations, aggregating BOLD
393 time series, tractography, computing structural connectivity, etc.) are made publicly available in the git repository served
394 at github.com/sina-mansour/UKB-connectomics. Additional scripts used to perform QC evaluations are also
395 provided in this repository. Furthermore, sample scripts to read the generated data into various programming languages are
396 made available to facilitate uptake of this resource by the community.

397 References

- 398 1. Valdés-Hernández, P. *et al.* Characterizing brain anatomical connections using diffusion weighted MRI and graph theory. *NeuroImage* **36**, 645–660, [10.1016/j.neuroimage.2007.02.012](https://doi.org/10.1016/j.neuroimage.2007.02.012) (2007).
- 399 2. Hagmann, P. *et al.* Mapping the Structural Core of Human Cerebral Cortex. *PLoS Biol.* **6**, e159, [10.1371/journal.pbio.0060159](https://doi.org/10.1371/journal.pbio.0060159) (2008).
- 400 3. van den Heuvel, M. P. & Hulshoff Pol, H. E. Exploring the brain network: A review on resting-state fMRI functional
401 connectivity. *Eur. Neuropsychopharmacol.* **20**, 519–534, [10.1016/j.euroneuro.2010.03.008](https://doi.org/10.1016/j.euroneuro.2010.03.008) (2010).
- 402 4. Smith, S. M. *et al.* Network modelling methods for fMRI. *NeuroImage* **54**, 875–891, [10.1016/j.neuroimage.2010.08.063](https://doi.org/10.1016/j.neuroimage.2010.08.063)
403 (2011).
- 404 5. Sporns, O. Making sense of brain network data. *Nat. Methods* **10**, 491–493, [10.1038/nmeth.2485](https://doi.org/10.1038/nmeth.2485) (2013).
- 405 6. Bullmore, E. & Sporns, O. Complex brain networks: Graph theoretical analysis of structural and functional systems. *Nat. Rev. Neurosci.* **10**, 186–198, [10.1038/nrn2575](https://doi.org/10.1038/nrn2575) (2009).
- 406 7. Van Essen, D. C. *et al.* The Human Connectome Project: A data acquisition perspective. *NeuroImage* **62**, 2222–2231,
407 [10.1016/j.neuroimage.2012.02.018](https://doi.org/10.1016/j.neuroimage.2012.02.018) (2012).
- 408 8. Alfaro-Almagro, F. *et al.* Image processing and Quality Control for the first 10,000 brain imaging datasets from UK
409 Biobank. *NeuroImage* **166**, 400–424, [10.1016/j.neuroimage.2017.10.034](https://doi.org/10.1016/j.neuroimage.2017.10.034) (2018).
- 410 9. Avesani, P. *et al.* The open diffusion data derivatives, brain data upcycling via integrated publishing of derivatives and
411 reproducible open cloud services. *Sci. Data* **6**, 69, [10.1038/s41597-019-0073-y](https://doi.org/10.1038/s41597-019-0073-y) (2019).
- 412 10. Mascarell Maričić, L. *et al.* The IMAGEN study: a decade of imaging genetics in adolescents. *Mol. Psychiatry* **25**,
413 2648–2671, [10.1038/s41380-020-0822-5](https://doi.org/10.1038/s41380-020-0822-5) (2020).
- 414 11. Karcher, N. R. & Barch, D. M. The ABCD study: understanding the development of risk for mental and physical health
415 outcomes. *Neuropsychopharmacology* **46**, 131–142, [10.1038/s41386-020-0736-6](https://doi.org/10.1038/s41386-020-0736-6) (2021).
- 416 12. Markiewicz, C. J. *et al.* The openneuro resource for sharing of neuroscience data. *eLife* **10**, [10.7554/eLife.71774](https://doi.org/10.7554/eLife.71774) (2021).
- 417 13. Sudlow, C. *et al.* UK Biobank: An Open Access Resource for Identifying the Causes of a Wide Range of Complex
418 Diseases of Middle and Old Age. *PLOS Medicine* **12**, e1001779, [10.1371/journal.pmed.1001779](https://doi.org/10.1371/journal.pmed.1001779) (2015).
- 419 14. Miller, K. L. *et al.* Multimodal population brain imaging in the UK Biobank prospective epidemiological study. *Nat. Neurosci.* **19**, 1523–1536, [10.1038/nn.4393](https://doi.org/10.1038/nn.4393) (2016).
- 420 15. Bycroft, C. *et al.* The UK Biobank resource with deep phenotyping and genomic data. *Nature* **562**, 203–209, [10.1038/s41586-018-0579-z](https://doi.org/10.1038/s41586-018-0579-z) (2018).
- 421 16. Jenkinson, M., Beckmann, C. F., Behrens, T. E., Woolrich, M. W. & Smith, S. M. FSL. *NeuroImage* **62**, 782–790,
422 [10.1016/j.neuroimage.2011.09.015](https://doi.org/10.1016/j.neuroimage.2011.09.015) (2012).
- 423 17. Van Essen, D. C. *et al.* The WU-Minn Human Connectome Project: An overview. *NeuroImage* **80**, 62–79, [10.1016/j.neuroimage.2013.05.041](https://doi.org/10.1016/j.neuroimage.2013.05.041) (2013).
- 424 18. Smith, S. M. Fast robust automated brain extraction. *Hum. Brain Mapp.* **17**, 143–155, [10.1002/hbm.10062](https://doi.org/10.1002/hbm.10062) (2002).
- 425 19. Jenkinson, M. & Smith, S. A global optimisation method for robust affine registration of brain images. *Med. Image
426 Analysis* **5**, 143–156, [10.1016/S1361-8415\(01\)00036-6](https://doi.org/10.1016/S1361-8415(01)00036-6) (2001).
- 427 20. Jenkinson, M., Bannister, P., Brady, M. & Smith, S. Improved Optimization for the Robust and Accurate Linear
428 Registration and Motion Correction of Brain Images. *NeuroImage* **17**, 825–841, [10.1006/nimg.2002.1132](https://doi.org/10.1006/nimg.2002.1132) (2002).
- 429 21. Andersson, J. L. R., Jenkinson, M. & Smith, S. Non-linear registration, aka spatial normalization. *FMRIB technical
430 report TR07JA2* (2010).
- 431 22. Zhang, Y., Brady, M. & Smith, S. Segmentation of brain MR images through a hidden Markov random field model and
432 the expectation–maximization algorithm. *IEEE Transactions on Med. Imaging* **20**, 45–57, [10.1109/42.906424](https://doi.org/10.1109/42.906424) (2001).
- 433 23. Patenaude, B., Smith, S. M., Kennedy, D. N. & Jenkinson, M. A Bayesian model of shape and appearance for subcortical
434 brain segmentation. *NeuroImage* **56**, 907–922, [10.1016/j.neuroimage.2011.02.046](https://doi.org/10.1016/j.neuroimage.2011.02.046) (2011).
- 435 24. Fischl, B. FreeSurfer. *NeuroImage* **62**, 774–781, [10.1016/j.neuroimage.2012.01.021](https://doi.org/10.1016/j.neuroimage.2012.01.021) (2012).
- 436 25. Moeller, S. *et al.* Multiband multislice GE-EPI at 7 tesla, with 16-fold acceleration using partial parallel imaging with
437 application to high spatial and temporal whole-brain fMRI. *Magn. Reson. Medicine* **63**, 1144–1153, [10.1002/mrm.22361](https://doi.org/10.1002/mrm.22361)
438 (2010).

445 26. Setsompop, K. *et al.* Blipped-controlled aliasing in parallel imaging for simultaneous multislice echo planar imaging with
446 reduced g-factor penalty. *Magn. Reson. Medicine* **67**, 1210–1224, [10.1002/mrm.23097](https://doi.org/10.1002/mrm.23097) (2012).

447 27. Preibisch, C., Castrillón G., J. G., Bührer, M. & Riedl, V. Evaluation of multiband EPI acquisitions for resting state fMRI.
448 *PLoS ONE* **10**, [10.1371/journal.pone.0136961](https://doi.org/10.1371/journal.pone.0136961) (2015).

449 28. Beckmann, C. & Smith, S. Probabilistic Independent Component Analysis for Functional Magnetic Resonance Imaging.
450 *IEEE Transactions on Med. Imaging* **23**, 137–152, [10.1109/TMI.2003.822821](https://doi.org/10.1109/TMI.2003.822821) (2004).

451 29. Salimi-Khorshidi, G. *et al.* Automatic denoising of functional MRI data: Combining independent component analysis
452 and hierarchical fusion of classifiers. *NeuroImage* **90**, 449–468, [10.1016/j.neuroimage.2013.11.046](https://doi.org/10.1016/j.neuroimage.2013.11.046) (2014).

453 30. Griffanti, L. *et al.* ICA-based artefact removal and accelerated fMRI acquisition for improved resting state network
454 imaging. *NeuroImage* **95**, 232–247, [10.1016/j.neuroimage.2014.03.034](https://doi.org/10.1016/j.neuroimage.2014.03.034) (2014).

455 31. Sotropoulos, S. N. *et al.* Advances in diffusion MRI acquisition and processing in the Human Connectome Project.
456 *NeuroImage* **80**, 125–143, [10.1016/j.neuroimage.2013.05.057](https://doi.org/10.1016/j.neuroimage.2013.05.057) (2013).

457 32. Andersson, J. L., Skare, S. & Ashburner, J. How to correct susceptibility distortions in spin-echo echo-planar images:
458 Application to diffusion tensor imaging. *NeuroImage* **20**, 870–888, [10.1016/S1053-8119\(03\)00336-7](https://doi.org/10.1016/S1053-8119(03)00336-7) (2003).

459 33. Andersson, J. L. & Sotropoulos, S. N. Non-parametric representation and prediction of single- and multi-shell diffusion-
460 weighted MRI data using Gaussian processes. *NeuroImage* **122**, 166–176, [10.1016/j.neuroimage.2015.07.067](https://doi.org/10.1016/j.neuroimage.2015.07.067) (2015).

461 34. Andersson, J. L. & Sotropoulos, S. N. An integrated approach to correction for off-resonance effects and subject
462 movement in diffusion MR imaging. *NeuroImage* **125**, 1063–1078, [10.1016/j.neuroimage.2015.10.019](https://doi.org/10.1016/j.neuroimage.2015.10.019) (2016).

463 35. Andersson, J. L., Graham, M. S., Zsoldos, E. & Sotropoulos, S. N. Incorporating outlier detection and replacement into a
464 non-parametric framework for movement and distortion correction of diffusion MR images. *NeuroImage* **141**, 556–572,
465 [10.1016/j.neuroimage.2016.06.058](https://doi.org/10.1016/j.neuroimage.2016.06.058) (2016).

466 36. Glasser, M. F. *et al.* The minimal preprocessing pipelines for the Human Connectome Project. *NeuroImage* **80**, 105–124,
467 [10.1016/j.neuroimage.2013.04.127](https://doi.org/10.1016/j.neuroimage.2013.04.127) (2013).

468 37. Basser, P., Mattiello, J. & Lebihan, D. Estimation of the Effective Self-Diffusion Tensor from the NMR Spin Echo. *J.
469 Magn. Reson. Ser. B* **103**, 247–254, [10.1006/jmrb.1994.1037](https://doi.org/10.1006/jmrb.1994.1037) (1994).

470 38. Zhang, H., Schneider, T., Wheeler-Kingshott, C. A. & Alexander, D. C. NODDI: Practical *in vivo* neurite orientation
471 dispersion and density imaging of the human brain. *NeuroImage* **61**, 1000–1016, [10.1016/j.neuroimage.2012.03.072](https://doi.org/10.1016/j.neuroimage.2012.03.072)
472 (2012).

473 39. Brett, M., Johnsrude, I. S. & Owen, A. M. The problem of functional localization in the human brain. *Nat. Rev. Neurosci.*
474 **3**, 243–249, [10.1038/nrn756](https://doi.org/10.1038/nrn756) (2002).

475 40. Fornito, A., Zalesky, A. & Breakspear, M. Graph analysis of the human connectome: Promise, progress, and pitfalls.
476 *NeuroImage* **80**, 426–444, [10.1016/j.neuroimage.2013.04.087](https://doi.org/10.1016/j.neuroimage.2013.04.087) (2013).

477 41. Zhang, F. *et al.* Quantitative mapping of the brain's structural connectivity using diffusion MRI tractography: A review.
478 *NeuroImage* **249**, 118870, [10.1016/j.neuroimage.2021.118870](https://doi.org/10.1016/j.neuroimage.2021.118870) (2022).

479 42. Sporns, O. The human connectome: Origins and challenges. *NeuroImage* **80**, 53–61, [10.1016/j.neuroimage.2013.03.023](https://doi.org/10.1016/j.neuroimage.2013.03.023)
480 (2013).

481 43. Bullmore, E. T. & Bassett, D. S. Brain Graphs: Graphical Models of the Human Brain Connectome. *Annu. Rev. Clin.
482 Psychol.* **7**, 113–140, [10.1146/annurev-clinpsy-040510-143934](https://doi.org/10.1146/annurev-clinpsy-040510-143934) (2011).

483 44. Tournier, J.-D. *et al.* MRtrix3: A fast, flexible and open software framework for medical image processing and visualisation.
484 *NeuroImage* **202**, 116137, [10.1016/j.neuroimage.2019.116137](https://doi.org/10.1016/j.neuroimage.2019.116137) (2019).

485 45. Zalesky, A. *et al.* Whole-brain anatomical networks: Does the choice of nodes matter? *NeuroImage* **50**, 970–983,
486 [10.1016/j.neuroimage.2009.12.027](https://doi.org/10.1016/j.neuroimage.2009.12.027) (2010).

487 46. Fornito, A., Zalesky, A. & Bullmore, E. T. Network scaling effects in graph analytic studies of human resting-state fMRI
488 data. *Front. Syst. Neurosci.* **4**, 1–16, [10.3389/fnsys.2010.00022](https://doi.org/10.3389/fnsys.2010.00022) (2010).

489 47. Schaefer, A. *et al.* Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI.
490 *Cereb. Cortex* **28**, 3095–3114, [10.1093/cercor/bhx179](https://doi.org/10.1093/cercor/bhx179) (2018).

491 48. Thomas Yeo, B. T. *et al.* The organization of the human cerebral cortex estimated by intrinsic functional connectivity. *J.
492 Neurophysiol.* **106**, 1125–1165, [10.1152/jn.00338.2011](https://doi.org/10.1152/jn.00338.2011) (2011).

493 49. Glasser, M. F. *et al.* A multi-modal parcellation of human cerebral cortex. *Nature* **536**, 171–178, [10.1038/nature18933](https://doi.org/10.1038/nature18933) (2016).

494 50. Desikan, R. S. *et al.* An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. *NeuroImage* **31**, 968–980, [10.1016/j.neuroimage.2006.01.021](https://doi.org/10.1016/j.neuroimage.2006.01.021) (2006).

495 51. Destrieux, C., Fischl, B., Dale, A. & Halgren, E. Automatic parcellation of human cortical gyri and sulci using standard anatomical nomenclature. *NeuroImage* **53**, 1–15, [10.1016/j.neuroimage.2010.06.010](https://doi.org/10.1016/j.neuroimage.2010.06.010) (2010).

496 52. Tian, Y., Margulies, D. S., Breakspear, M. & Zalesky, A. Topographic organization of the human subcortex unveiled with functional connectivity gradients. *Nat. Neurosci.* **23**, 1421–1432, [10.1038/s41593-020-00711-6](https://doi.org/10.1038/s41593-020-00711-6) (2020).

497 53. Marcus, D. S. *et al.* Human Connectome Project informatics: Quality control, database services, and data visualization. *NeuroImage* **80**, 202–219, [10.1016/j.neuroimage.2013.05.077](https://doi.org/10.1016/j.neuroimage.2013.05.077) (2013).

498 54. Brett, M. *et al.* nipy/nibabel. *Zenodo* [10.5281/zenodo.591597](https://zenodo.5281/zenodo.591597) (2020).

499 55. Li, K., Guo, L., Nie, J., Li, G. & Liu, T. Review of methods for functional brain connectivity detection using fMRI. *Comput. Med. Imaging Graph.* **33**, 131–139, [10.1016/j.compmedimag.2008.10.011](https://doi.org/10.1016/j.compmedimag.2008.10.011) (2009).

500 56. Saad, Z. S. *et al.* Trouble at Rest: How Correlation Patterns and Group Differences Become Distorted After Global Signal Regression. *Brain Connect.* **2**, 25–32, [10.1089/brain.2012.0080](https://doi.org/10.1089/brain.2012.0080) (2012).

501 57. Yan, C. G., Craddock, R. C., Zuo, X. N., Zang, Y. F. & Milham, M. P. Standardizing the intrinsic brain: Towards robust measurement of inter-individual variation in 1000 functional connectomes. *NeuroImage* **80**, 246–262, [10.1016/j.neuroimage.2013.04.081](https://doi.org/10.1016/j.neuroimage.2013.04.081) (2013).

502 58. Gotts, S. J. *et al.* The perils of global signal regression for group comparisons: A case study of Autism Spectrum Disorders. *Front. Hum. Neurosci.* **7**, 1–20, [10.3389/fnhum.2013.00356](https://doi.org/10.3389/fnhum.2013.00356) (2013).

503 59. Murphy, K. & Fox, M. D. Towards a consensus regarding global signal regression for resting state functional connectivity MRI. *NeuroImage* **154**, 169–173, [10.1016/j.neuroimage.2016.11.052](https://doi.org/10.1016/j.neuroimage.2016.11.052) (2017).

504 60. Liu, T. T., Nalci, A. & Falahpour, M. The global signal in fMRI: Nuisance or Information? *NeuroImage* **150**, 213–229, [10.1016/j.neuroimage.2017.02.036](https://doi.org/10.1016/j.neuroimage.2017.02.036) (2017).

505 61. Power, J. D., Plitt, M., Laumann, T. O. & Martin, A. Sources and implications of whole-brain fMRI signals in humans. *NeuroImage* **146**, 609–625, [10.1016/j.neuroimage.2016.09.038](https://doi.org/10.1016/j.neuroimage.2016.09.038) (2017).

506 62. Billings, J. & Keilholz, S. The Not-So-Global Blood Oxygen Level-Dependent Signal. *Brain Connect.* **8**, 121–128, [10.1089/brain.2017.0517](https://doi.org/10.1089/brain.2017.0517) (2018).

507 63. Li, J. *et al.* Global signal regression strengthens association between resting-state functional connectivity and behavior. *NeuroImage* **196**, 126–141, [10.1016/j.neuroimage.2019.04.016](https://doi.org/10.1016/j.neuroimage.2019.04.016) (2019).

508 64. Aquino, K. M., Fulcher, B. D., Parkes, L., Sabaroedin, K. & Fornito, A. Identifying and removing widespread signal deflections from fMRI data: Rethinking the global signal regression problem. *NeuroImage* **212**, 116614, [10.1016/j.neuroimage.2020.116614](https://doi.org/10.1016/j.neuroimage.2020.116614) (2020).

509 65. Tournier, J. D., Calamante, F., Gadian, D. G. & Connelly, A. Direct estimation of the fiber orientation density function from diffusion-weighted MRI data using spherical deconvolution. *NeuroImage* **23**, 1176–1185, [10.1016/j.neuroimage.2004.07.037](https://doi.org/10.1016/j.neuroimage.2004.07.037) (2004).

510 66. Dhollander, T., Raffelt, D. & Connelly, A. Unsupervised 3-tissue response function estimation from single-shell or multi-shell diffusion MR data without a co-registered T1 image. In *ISMRM Workshop on Breaking the Barriers of Diffusion MRI*, 5 (2016).

511 67. Dhollander, T., Mito, R., Raffelt, D. & Connelly, A. Improved white matter response function estimation for 3-tissue constrained spherical deconvolution. *Proc. Intl. Soc. Mag. Reson. Med.* **555** (2019).

512 68. Jeurissen, B., Tournier, J. D., Dhollander, T., Connelly, A. & Sijbers, J. Multi-tissue constrained spherical deconvolution for improved analysis of multi-shell diffusion MRI data. *NeuroImage* **103**, 411–426, [10.1016/j.neuroimage.2014.07.061](https://doi.org/10.1016/j.neuroimage.2014.07.061) (2014).

513 69. Dhollander, T. *et al.* Multi-tissue log-domain intensity and inhomogeneity normalisation for quantitative apparent fibre density. *Proc. ISMRM* **29**, 2472 (2021).

514 70. Smith, R. E., Tournier, J. D., Calamante, F. & Connelly, A. Anatomically-constrained tractography: Improved diffusion MRI streamlines tractography through effective use of anatomical information. *NeuroImage* **62**, 1924–1938, [10.1016/j.neuroimage.2012.06.005](https://doi.org/10.1016/j.neuroimage.2012.06.005) (2012).

542 71. Tournier, J. D., Calamante, F. & Connelly, A. Improved probabilistic streamlines tractography by 2nd order integration
543 over fibre orientation distributions. *Isrrm* **88**, 2010 (2010).

544 72. Smith, R., Raffelt, D., Tournier, J.-D. & Connelly, A. Quantitative streamlines tractography: methods and inter-subject
545 normalisation. *Aperture Neuro* **2**, 1–23, [10.52294/ApertureNeuro.2022.2.NEOD9565](https://doi.org/10.52294/ApertureNeuro.2022.2.NEOD9565) (2022).

546 73. Mansour L, S., Tian, Y., Yeo, B. T., Cropley, V. & Zalesky, A. High-resolution connectomic fingerprints: Mapping neural
547 identity and behavior. *NeuroImage* **229**, 117695, [10.1016/j.neuroimage.2020.117695](https://doi.org/10.1016/j.neuroimage.2020.117695) (2021).

548 74. Mansour L, S., Seguin, C., Smith, R. E. & Zalesky, A. Connectome spatial smoothing (CSS): Concepts, methods, and
549 evaluation. *NeuroImage* **250**, 118930, [10.1016/j.neuroimage.2022.118930](https://doi.org/10.1016/j.neuroimage.2022.118930) (2022).

550 75. Meade, B., Lafayette, L., Sauter, G. & Tosello, D. Spartan HPC-Cloud Hybrid: Delivering Performance and Flexibility,
551 [10.4225/49/58ead90dceaaa](https://doi.org/10.4225/49/58ead90dceaaa) (2017).

552 76. Lafayette, L. & Wiebelt, B. Spartan and NEMO: Two HPC-cloud hybrid implementations. *Proc. - 13th IEEE Int. Conf.*
553 *on eScience, eScience 2017* 458–459, [10.1109/eScience.2017.70](https://doi.org/10.1109/eScience.2017.70) (2017).

554 77. Sotiropoulos, S. N. & Zalesky, A. Building connectomes using diffusion MRI: why, how and but. *NMR Biomed.* **32**,
555 1–23, [10.1002/nbm.3752](https://doi.org/10.1002/nbm.3752) (2019).

556 78. Welvaert, M. & Rosseel, Y. On the definition of signal-to-noise ratio and contrast-to-noise ratio for fMRI data. *PLoS*
557 *ONE* **8**, [10.1371/journal.pone.0077089](https://doi.org/10.1371/journal.pone.0077089) (2013).

558 79. Garrett, D. D., Kovacevic, N., McIntosh, A. R. & Grady, C. L. Blood oxygen level-dependent signal variability is more
559 than just noise. *J. Neurosci.* **30**, 4914–4921, [10.1523/JNEUROSCI.5166-09.2010](https://doi.org/10.1523/JNEUROSCI.5166-09.2010) (2010).

560 80. Garrett, D. D., Kovacevic, N., McIntosh, A. R. & Grady, C. L. The importance of being variable. *J. Neurosci.* **31**,
561 4496–4503, [10.1523/JNEUROSCI.5641-10.2011](https://doi.org/10.1523/JNEUROSCI.5641-10.2011) (2011).

562 81. Jezzard, P. & Clare, S. Sources of distortion in functional MRI data. *Hum. Brain Mapp.* **8**, 80–85, [10.1002/\(SICI\)1097-0193\(1999\)8:2<80::AID-HBM2>3.0.CO;2-C](https://doi.org/10.1002/(SICI)1097-0193(1999)8:2<80::AID-HBM2>3.0.CO;2-C) (1999).

563 82. Stenger, V. A. Technical considerations for BOLD fMRI of the orbitofrontal cortex. In *The Orbitofrontal Cortex*, 423–446,
564 [10.1093/acprof:oso/9780198565741.003.0017](https://doi.org/10.1093/acprof:oso/9780198565741.003.0017) (Oxford University PressOxford, 2006).

565 83. Jbabdi, S. & Johansen-Berg, H. Tractography: Where Do We Go from Here? *Brain Connect.* **1**, 169–183, [10.1089/brain.2011.0033](https://doi.org/10.1089/brain.2011.0033) (2011).

566 84. Roberts, J. A., Perry, A., Roberts, G., Mitchell, P. B. & Breakspear, M. Consistency-based thresholding of the human
567 connectome. *NeuroImage* **145**, 118–129, [10.1016/j.neuroimage.2016.09.053](https://doi.org/10.1016/j.neuroimage.2016.09.053) (2017).

568 85. Fornito, A., Zalesky, A. & Bullmore, E. T. *Fundamentals of Brain Network Analysis* (Elsevier, 2016).

569 86. Gong, G. *et al.* Mapping anatomical connectivity patterns of human cerebral cortex using in vivo diffusion tensor imaging
570 tractography. *Cereb. Cortex* **19**, 524–536, [10.1093/cercor/bhn102](https://doi.org/10.1093/cercor/bhn102) (2009).

571 87. Bassett, D. S. & Bullmore, E. Small-world brain networks. *Neuroscientist* **12**, 512–523, [10.1177/1073858406293182](https://doi.org/10.1177/1073858406293182)
572 (2006).

573 88. Achard, S., Salvador, R., Whitcher, B., Suckling, J. & Bullmore, E. A resilient, low-frequency, small-world human
574 brain functional network with highly connected association cortical hubs. *J. Neurosci.* **26**, 63–72, [10.1523/JNEUROSCI.3874-05.2006](https://doi.org/10.1523/JNEUROSCI.3874-05.2006) (2006).

575 89. Iturria-Medina, Y., Sotero, R. C., Canales-Rodríguez, E. J., Alemán-Gómez, Y. & Melie-García, L. Studying the human
576 brain anatomical network via diffusion-weighted MRI and Graph Theory. *NeuroImage* **40**, 1064–1076, [10.1016/j.neuroimage.2007.10.060](https://doi.org/10.1016/j.neuroimage.2007.10.060) (2008).

577 90. Hayasaka, S. & Laurienti, P. J. Comparison of characteristics between region-and voxel-based network analyses in
578 resting-state fMRI data. *NeuroImage* **50**, 499–508, [10.1016/j.neuroimage.2009.12.051](https://doi.org/10.1016/j.neuroimage.2009.12.051) (2010).

579 91. Joyce, K. E., Laurienti, P. J., Burdette, J. H. & Hayasaka, S. A new measure of centrality for brain networks. *PLoS ONE*
580 **5**, [10.1371/journal.pone.0012200](https://doi.org/10.1371/journal.pone.0012200) (2010).

581 92. Honey, C. J., Kötter, R., Breakspear, M. & Sporns, O. Network structure of cerebral cortex shapes functional connectivity
582 on multiple time scales. *Proc. Natl. Acad. Sci. United States Am.* **104**, 10240–10245, [10.1073/pnas.0701519104](https://doi.org/10.1073/pnas.0701519104) (2007).

583 93. van den Heuvel, M. P., Mandl, R. C., Kahn, R. S. & Hulshoff Pol, H. E. Functionally linked resting-state networks
584 reflect the underlying structural connectivity architecture of the human brain. *Hum. Brain Mapp.* **30**, 3127–3141,
585 [10.1002/hbm.20737](https://doi.org/10.1002/hbm.20737) (2009).

590 94. Honey, C. J. *et al.* Predicting human resting-state functional connectivity from structural connectivity. *Proc. Natl. Acad. Sci. United States Am.* **106**, 2035–2040, [10.1073/pnas.0811168106](https://doi.org/10.1073/pnas.0811168106) (2009).

591 95. Honey, C. J., Thivierge, J. P. & Sporns, O. Can structure predict function in the human brain? *NeuroImage* **52**, 766–776, [10.1016/j.neuroimage.2010.01.071](https://doi.org/10.1016/j.neuroimage.2010.01.071) (2010).

592 96. Vázquez-Rodríguez, B. *et al.* Gradients of structure–function tethering across neocortex. *Proc. Natl. Acad. Sci. United States Am.* **116**, 21219–21227, [10.1073/pnas.1903403116](https://doi.org/10.1073/pnas.1903403116) (2019).

593 97. Preti, M. G. & Van De Ville, D. Decoupling of brain function from structure reveals regional behavioral specialization in humans. *Nat. Commun.* **10**, 1–7, [10.1038/s41467-019-12765-7](https://doi.org/10.1038/s41467-019-12765-7) (2019).

594 98. Suárez, L. E., Markello, R. D., Betzel, R. F. & Misic, B. Linking Structure and Function in Macroscale Brain Networks. *Trends Cogn. Sci.* **24**, 302–315, [10.1016/j.tics.2020.01.008](https://doi.org/10.1016/j.tics.2020.01.008) (2020).

595 99. Baum, G. L. *et al.* Development of structure–function coupling in human brain networks during youth. *Proc. Natl. Acad. Sci.* **117**, 771–778, [10.1073/pnas.1912034117](https://doi.org/10.1073/pnas.1912034117) (2020).

600 100. Estrada, E. & Hatano, N. Communicability in complex networks. *Phys. Rev. E - Stat. Nonlinear, Soft Matter Phys.* **77**, 1–12, [10.1103/PhysRevE.77.036111](https://doi.org/10.1103/PhysRevE.77.036111) (2008).

601 101. Margulies, D. S. *et al.* Situating the default-mode network along a principal gradient of macroscale cortical organization. *Proc. Natl. Acad. Sci.* **113**, 12574–12579, [10.1073/pnas.1608282113](https://doi.org/10.1073/pnas.1608282113) (2016).

602 102. Rubinov, M. & Sporns, O. Complex network measures of brain connectivity: Uses and interpretations. *NeuroImage* **52**, 1059–1069, [10.1016/j.neuroimage.2009.10.003](https://doi.org/10.1016/j.neuroimage.2009.10.003) (2010).

603 103. Hagberg, A., Swart, P. & Chult, D. S. Exploring network structure, dynamics, and function using NetworkX (2008).

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614 Author contributions statement

615 **S.M.L.**: Pipeline development, Software, Data curation, Formal analysis, Writing - original draft, Writing - review & editing.
616 **M.D.B.**: Pipeline development, Writing - original draft, Writing - review & editing. **R.S.**: Pipeline development, Software,
617 Writing - original draft, Writing - review & editing. **A.Z.**: Supervision, Pipeline development, Software, Writing - original draft,
618 Writing - review & editing. **C.S.**: Supervision, Funding acquisition, Pipeline development, Writing - original draft, Writing -
619 review & editing.

620 Competing interests

621 The authors declare no competing interests.

622 **Supplementary Information**

623 Comprehensive directory tree

624 A summarized directory tree was provided in the main text to list all released data. Figure S1 provides an extensive list of all
625 files provided in the compressed archives of a session.

Figure S1. Complete list of all files included in provided archives. Three separate compressed archives are provided, for each of atlas parcellation (\rightarrow atlas/*), functional time series (\rightarrow fMRI/*), and structural connectivity (\rightarrow tractography/*) pipelines.

626 **Resting-state signal loss**

627 The BOLD signal was collected using a gradient echo EPI acquisition which can experience geometric distortion as well as
628 signal loss in regions of strong susceptibility⁸¹. Computing a brain mask from empirical fMRI data, using any method based on
629 image intensity, may lead to exclusion of such regions. All voxels outside of this brain mask were explicitly zero-filled in UKB
630 fMRI preprocessing pipeline⁸. For a region that can be clearly delineated on an effectively undistorted anatomical image, but
631 its entire volume resides outside of the fMRI brain mask, the aggregate fMRI signal within that region would consequently be
632 zero-filled. These cases can be identified by computing the QC measure of regional signal variance. Hence, signal variance can
633 be used as a proxy to assess signal loss due to exclusion of susceptible regions.

634 To evaluate the cases in which UKB preprocessing led to such problems, we counted the number of sessions for which a
635 variance of zero (constant signal) was reported for a brain region. This information was then sorted to pinpoint the regions
636 with highest detrimental impact of signal loss. Table S1 provides a list of percentages of signal loss for 100 mostly affected
637 brain regions (across different atlases) sorted based on signal loss severity. This indicated a pattern of severe signal loss within
638 the orbitofrontal cortex (OFC). The signal loss severity was higher for higher granularity levels such that the cortical atlases
639 with 1000 regions had signal loss in more than a third of the cohort. However, the severity was considerably lower for lower
640 granularities such that atlases with fewer than 700 regions had signal loss in less than 5% of the cohort.

641 We hereby report this issue as a limitation of the fMRI acquisition and preprocessing and suggest either i) conducting
642 the analysis at lower granularities (especially if OFC is of interest), or ii) excluding the impacted regions of OFC
643 in cases where the analyses are to be conducted on higher granularities. Finally, to verify that signal loss was due to
644 impacts of preprocessing on OFC and not a result of the connectivity mapping pipeline manual visual inspections were
645 conducted for a handful of sessions. Figure S2 provides an example that shows a complete lack of signal in the OFC parcel
646 (Schaefer7n1000p:7Networks_LH_Limbic_OFC_6) due to zero-filling leading to a zero variance QC metric.

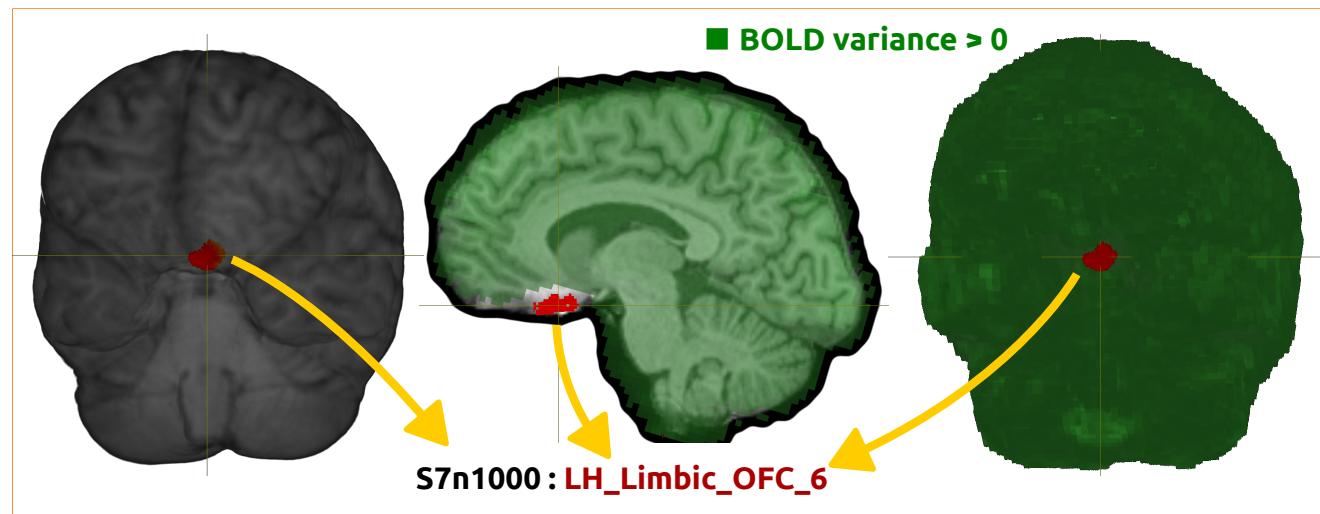


Figure S2. Illustration of signal loss near certain OFC regions for a single session. The LH_Limbic_OFC_6 regions from S7n1000 atlas is highlighted (red) on a 3D rendered T1 brain [left]. A sagittal slice of the brain showing the same parcel (red) along with a highlighted map of regions within the rfMRI brain mask (green) for which signal variance is positive [middle]. A similar 3D render showing the particular OFC parcel falling outside of the fMRI mask [right]. The images indicate that the preprocessed fMRI signal fails to cover certain cortical gray matter regions belonging to the OFC.

Table S1. One hundred regions that were most severely affected by BOLD signal loss. The percentage of sessions for which zero variance was recorded in a certain region was quantified. This quantifies the frequency by which a region falls outside of the fMRI brain mask due to effects of signal loss.

Signal loss Table	
Atlas:Parcel	Percentage of signal loss (over all sessions)
Schaefer7n1000p:7Networks_LH_Limbic_OFC_6	36.5
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_6	36.5
Schaefer7n1000p:7Networks_LH_Limbic_OFC_3	15
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_3	15
Schaefer7n1000p:7Networks_RH_Limbic_OFC_4	13.6
Schaefer7n900p:7Networks_RH_Limbic_OFC_4	13.6
Schaefer17n1000p:17Networks_RH_LimbicB_OFC_4	13.6
Schaefer17n900p:17Networks_RH_LimbicB_OFC_4	13.6
Schaefer17n900p:17Networks_LH_LimbicB_OFC_7	11.4
Schaefer7n900p:7Networks_LH_Limbic_OFC_7	11.4
Schaefer7n1000p:7Networks_LH_Limbic_OFC_11	10.2
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_11	10.2
Schaefer17n800p:17Networks_LH_LimbicB_OFC_7	8.4
Schaefer7n800p:7Networks_LH_Limbic_OFC_7	8.4
Schaefer7n1000p:7Networks_LH_Limbic_OFC_2	7.9
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_2	7.9
Schaefer7n600p:7Networks_RH_Limbic_OFC_2	7.5
Schaefer17n600p:17Networks_RH_LimbicB_OFC_2	7.5
Schaefer17n700p:17Networks_RH_LimbicB_OFC_2	7.5
Schaefer7n700p:7Networks_RH_Limbic_OFC_2	7.5
Schaefer17n800p:17Networks_RH_LimbicB_OFC_2	6.6
Schaefer7n800p:7Networks_RH_Limbic_OFC_2	6.6
Schaefer7n800p:7Networks_RH_Limbic_OFC_7	6.3
Schaefer17n800p:17Networks_RH_LimbicB_OFC_9	6.3
Schaefer7n900p:7Networks_RH_Limbic_OFC_3	6.3
Schaefer17n900p:17Networks_RH_LimbicB_OFC_3	6.3
Schaefer7n1000p:7Networks_LH_Limbic_OFC_4	6.3
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_4	6.3
Schaefer7n1000p:7Networks_RH_Limbic_OFC_8	6.2
Schaefer17n1000p:17Networks_RH_LimbicB_OFC_10	6.2
Schaefer17n700p:17Networks_LH_LimbicB_OFC_1	5.8
Schaefer7n700p:7Networks_LH_Limbic_OFC_1	5.8
Schaefer7n900p:7Networks_LH_Limbic_OFC_1	5.4
Schaefer17n900p:17Networks_LH_LimbicB_OFC_1	5.4
Schaefer7n800p:7Networks_RH_Limbic_OFC_4	5.3
Schaefer17n800p:17Networks_RH_LimbicB_OFC_4	5.3
Schaefer7n900p:7Networks_RH_Limbic_OFC_8	5.3
Schaefer17n900p:17Networks_RH_LimbicB_OFC_8	5.3
Schaefer7n700p:7Networks_LH_Limbic_OFC_3	4.5
Schaefer17n700p:17Networks_LH_LimbicB_OFC_3	4.5
Schaefer7n1000p:7Networks_RH_Limbic_OFC_3	3.9
Schaefer17n1000p:17Networks_RH_LimbicB_OFC_3	3.9
Schaefer7n600p:7Networks_RH_Limbic_OFC_6	3.9
Schaefer17n600p:17Networks_RH_LimbicB_OFC_7	3.9
Schaefer7n800p:7Networks_RH_Limbic_OFC_3	3.7
Schaefer17n800p:17Networks_RH_LimbicB_OFC_3	3.7
Schaefer7n900p:7Networks_LH_Limbic_OFC_3	3.2
Schaefer17n900p:17Networks_LH_LimbicB_OFC_3	3.2
Schaefer17n800p:17Networks_LH_LimbicB_OFC_2	2.9

Continuation of signal loss Table S1	
Atlas:Parcel	Percentage of signal loss (over all sessions)
Schaefer7n800p:7Networks_LH_Limbic_OFC_2	2.9
Schaefer7n700p:7Networks_RH_Limbic_OFC_3	2.6
Schaefer17n700p:17Networks_RH_LimbicB_OFC_3	2.6
Schaefer7n600p:7Networks_RH_Limbic_OFC_3	2.6
Schaefer17n600p:17Networks_RH_LimbicB_OFC_3	2.6
Schaefer7n700p:7Networks_LH_Limbic_OFC_5	2.6
Schaefer17n700p:17Networks_LH_LimbicB_OFC_5	2.6
Schaefer17n600p:17Networks_LH_LimbicB_OFC_4	2.5
Schaefer7n600p:7Networks_LH_Limbic_OFC_4	2.5
Schaefer17n800p:17Networks_LH_LimbicB_OFC_11	2.4
Schaefer7n800p:7Networks_LH_Limbic_OFC_10	2.4
Glasser:L_pOFC_ROI	2.4
Schaefer17n800p:17Networks_LH_LimbicB_OFC_4	2
Schaefer7n800p:7Networks_LH_Limbic_OFC_4	2
Schaefer7n500p:7Networks_RH_Limbic_OFC_2	1.9
Schaefer17n500p:17Networks_RH_LimbicB_OFC_2	1.9
Schaefer7n800p:7Networks_RH_Limbic_OFC_9	1.6
Schaefer7n400p:7Networks_RH_Limbic_OFC_5	1.6
Schaefer17n800p:17Networks_RH_LimbicB_OFC_11	1.6
Schaefer17n400p:17Networks_RH_LimbicB_OFC_5	1.6
Schaefer7n400p:7Networks_LH_Limbic_OFC_1	1.4
Schaefer17n400p:17Networks_LH_LimbicB_OFC_1	1.4
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_12	1.3
Schaefer7n1000p:7Networks_LH_Limbic_OFC_12	1.3
Schaefer17n500p:17Networks_LH_LimbicB_OFC_1	1.3
Schaefer7n500p:7Networks_LH_Limbic_OFC_1	1.3
Schaefer17n600p:17Networks_LH_LimbicB_OFC_2	1.2
Schaefer7n600p:7Networks_LH_Limbic_OFC_2	1.2
Schaefer7n1000p:7Networks_LH_Limbic_OFC_1	1.2
Schaefer17n1000p:17Networks_LH_LimbicB_OFC_1	1.2
Schaefer7n900p:7Networks_RH_Limbic_OFC_2	1.2
Schaefer17n1000p:17Networks_RH_LimbicB_OFC_2	1.2
Schaefer7n1000p:7Networks_RH_Limbic_OFC_2	1.2
Schaefer7n800p:7Networks_LH_Limbic_OFC_1	0.9
Schaefer17n800p:17Networks_LH_LimbicB_OFC_1	0.9
Schaefer17n1000p:17Networks_RH_LimbicB_OFC_5	0.8
Schaefer7n1000p:7Networks_RH_Limbic_OFC_5	0.8
Glasser:R_25_ROI	0.8
Schaefer7n900p:7Networks_RH_Limbic_OFC_5	0.7
Schaefer17n900p:17Networks_RH_LimbicB_OFC_5	0.7
Schaefer17n900p:17Networks_RH_LimbicA_TempPole_2	0.7
Schaefer7n900p:7Networks_RH_Limbic_TempPole_2	0.7
Glasser:L_25_ROI	0.6
Schaefer17n700p:17Networks_RH_LimbicB_OFC_4	0.6
Schaefer7n700p:7Networks_RH_Limbic_OFC_4	0.6
Schaefer7n500p:7Networks_LH_Limbic_OFC_5	0.5
Schaefer17n500p:17Networks_LH_LimbicB_OFC_5	0.5
Schaefer17n900p:17Networks_LH_LimbicA_TempPole_7	0.5
Schaefer7n900p:7Networks_LH_Limbic_TempPole_7	0.5
Schaefer7n700p:7Networks_LH_Limbic_TempPole_12	0.5