The Human Connectome Project rfMRI Repository Manual

Important: If you use the scripts, or approach set out in this manual, you can use the boilerplate text provided in Appendix 1 and reference the Github repository and Zenodo dataset appropriately.

This manual aims to provide more information about the processing steps used to create functional time series and Pearson correlation functional connectivity matrices for the *resting-state fMRI scans* provided by the Human Connectome Project (HCP). It is applicable to two different HCP databases: the HCP-Young Adult database and the HCP-Aging database. This manual serves as an accompaniment to the scripts provided in the repository https://github.com/floristijhuis/HCP-rfMRI-repository and the connectivity matrices provided in the Zenodo dataset release of this project that can be found here: https://doi.org/10.5281/zenodo.6770120.

Databases

1. *HCP-Aging*

The HCP-Aging project aims to provide comprehensive neuroimaging data for >1500 subjects aged 35-100 (Bookheimer et al., 2019), with a subset of these subjects being tested longitudinally. In addition to T1w-images, T2w-images, and DTI, several functional MRI scans were made for each subject: 2 resting-state fMRI scans as well as task-based fMRI scans (Go/NoGo task, a visuomotor task, and Face-Name matching memory task). Moreover, the subjects underwent a wide range of biological, genetic, and behavioral tests, described in detail in (Bookheimer et al., 2019). In February 2021, the first batch (725 subjects tested cross-sectionally) was released. The next release (including more cross-sectional data and longitudinal data) is expected in Fall 2022.

2. *HCP-Young Adult*

The HCP-Young Adult database was the original HCP database and contains brain data for 1200 healthy subjects aged 21-35 (van Essen et al., 2013). The data in this database are somewhat more extensive than those provided for the HCP-Aging database; for instance, the scanning time for the rfMRI scans is longer (14 minutes instead of 6.5) and it includes 7 task-based fMRI scans (working memory, reward processing, motor processing, language, social cognition, relational processing, emotional processing). Moreover, some subjects have additional 7T MRI data or MEG data. On the other hand, it is also a relatively homogeneous group, which can be good for some purposes (e.g. testing new hypotheses on the connectivity structure of the brain) but may be suboptimal for others (e.g. in clinical neuroscience research, in which a wider and more ecologically valid sample like the HCP-Aging database may be preferable).

Due to privacy limitations, not all files can be made publicly accessible (e.g. the behavioral data of each subject). In order to run all the scripts and make full use of the data (e.g. if you want to obtain the time series or want to access behavioral data) you will need to request access to the HCP data yourself. For the HCP-Aging database, you will need to request access to the NDA database containing the HCP data and create an account on the NDA website when access has been granted (for more information, refer to this file).[1] For the HCP-Young Adult database, you only need to create an account on Connectome DB and accept the data use conditions (for information, refer to this link).

[1] The requirements for access to the NDA are relatively strict. For instance, you need to be associated to a research institution and have a research-related need to access the data.

HCP Data and processing

The current section describes in more detail the HCP data structure, the preprocessing performed by the HCP creators, and the additional processing steps and choices made in the current project in order to obtain rfMRI time series and connectivity matrices for both databases.

1. *The CIFTI format*

All HCP files use the CIFTI data structure in order to store high-quality neuroimaging data in a computationally efficient way. The CIFTI format allows for the mapping of this data to the cortical surface, leading to a more accurate localization of the signal and preventing common issues arising from, for instance, volume-based smoothing procedures (Brodoehl et al., 2020; Coalson et al., 2018; Glasser et al., 2013). Instead of using voxels, the CIFTI format uses cortical surface vertices and subcortical voxels ("grayordinates") as its basic spatial units. There are different software packages available to work with CIFTI files: Connectome Workbench (developed by the HCP, including wb_command for command-line handling and processing of CIFTI files and wb_view for visualization purposes), ciftiTools (made for handling CIFTI files in R), and cifti-matlab (made for handling CIFTI files in MATLAB). Some relevant CIFTI file types used in this project are .dtseries.nii files for surface-based time series and .dlabel.nii for surface-based atlases.

2. *Processing performed by the HCP*

The Human Connectome Project has developed its own 'minimal preprocessing pipeline' which performs some basic preprocessing steps using surface-based algorithms (Glasser et al., 2013). Although there are minor differences between the processing performed in the HCP-Young Adult and the HCP-Aging database, the majority has remained constant.

Briefly, the *fMRIVolume* pipeline performs some basic preprocessing steps on the raw fMRI scan in volume space, including gradient nonlinearity distortion correction, 12-motion-parameter frame realignment, susceptibility distortion correction using FSL topup, and registration to MNI space, after which intensity normalization (mean intensity of 10000) and brain masking is performed. *fMRISurface* maps the activity from volume space to the cortical surface and performs 2mm Gaussian smoothing on the surface. After this, *ICA-FIX* was used as an ICA-based tool to remove artefacts and noise in the data (using surface-based data) (Glasser et al., 2013).[2] Lastly, the *MSMAII* pipeline was employed to align the individual functional scan to a group template. The *MSMAII* pipeline uses multimodal data (T1w/T2w myelin maps, resting-state network and visuotopic maps) for accurate cross-subject alignment of functional data (Robinson et al., 2018). The creators of the HCP-Aging database highly recommend using their preprocessing pipeline without any changes (see here, here), so this approach was taken in the current project.

3. *Additional processing*

Each of the two resting-state scans consisted of two 6.5-minute (HCP-Aging) or 14-minute (HCP-Young Adult) separate sub-scans. These separate sub-scans were obtained using two different phase-encoding directions (anterior-posterior and posterior-anterior for HCP-Aging and left-right and right-left for HCP-Young Adult) and preprocessed separately. In order to be able to concatenate these discontinuous scans, they needed to be demeaned and variance-normalized first in order to standardize them (for reference, see here, here (Q3), and Figure 1). Next, they were concatenated.

[2] The settings for ICA-FIX differed slightly between the HCP-Young Adult and the HCP-Aging database. For instance, for the HCP-Young Adult it included a linear detrend and motion parameter regression, whereas it only included a linear effective detrend without temporal filtering in the HCP Aging scans.

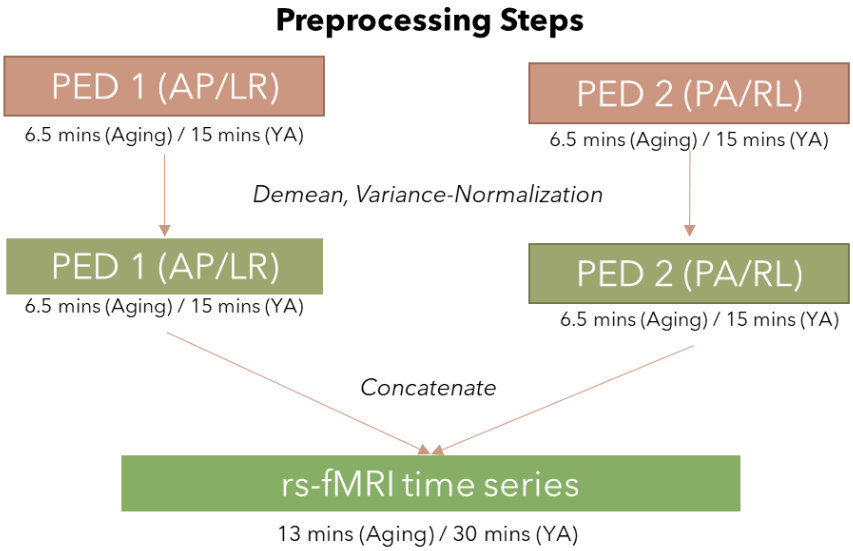

Figure 1: An illustration of the demeaning and variance normalization step prior to the concatenation of the individual rfMRI subscans. PED=Phase Encoding Direction; AP = anterior-posterior; LR = left-right; PA = posterior-anterior; RL = right-left; YA = HCP-Young Adult. Depending on your research question, this pipeline may be adapted in order to also include the other full resting state scan in order to generate one scan for each participant consisting of 4 separate rfMRI runs.

4. *Parcellation and atlases*

The next step was to parcellate the data using a brain atlas, in order to get a time series for each individual brain region in your atlas and a corresponding Pearson correlation connectivity matrix. Different research questions require different types of atlases. Therefore, several different types of atlases were used to parcellate the data and generate the average time series in a set of given brain regions. The following section intends to briefly explain the atlas choice and highlight generally important aspects of atlas selection.

General remarks

There are several different reasons for using a multitude of functional atlases. For instance, the type of intended network analysis and its computational demands provide constraints on the maximal resolution that can be used. Some analyses may require a low resolution whereas others benefit from a high resolution, and yet others may profit from a comparison between results obtained from both low-resolution and high-resolution atlases. Different types of atlases with a similar resolution may also be used within the same study for validation purposes.

When considering atlas quality, it is important that functional region boundaries are respected. Another requirement is that the cortical part of the atlas exists as a surface-based atlas. Ideally, the initial construction of the atlas should also be performed in surface-space, which has significantly better registration accuracy across subjects for functional data (Schaefer et al., 2018). An atlas like the Automatic Anatomical Labeling (AAL) atlas was not included here, as this atlas is minimally related to functional boundaries and was also not constructed in surface space.

Lastly, surface-based atlases do not include subcortical regions, as surface analysis is only applicable to the cortical surface. In case one wants to include subcortical structures in their analysis as well, a matching of a cortical and subcortical atlas needs to occur. The cortical atlases that were chosen, as well as their matching to subcortical atlases can be found in Figure 2. More information about how the atlases were constructed and their annotation files can be found in the /Atlases folder of the Github of this project. In the following, I will describe the reasons for the atlas selection for this project.

Atlas Selection – Cortex

1. *Glasser*

The Glasser MMP 1.0 atlas is the primary atlas recommended for analyses by the creators of the Human Connectome Project (Glasser et al., 2017). It consists of 360 cortical regions that were delimited based on multimodal data (T1w/T2w, resting-state fMRI and task-based fMRI) collected from HCP subjects. Due to the multimodal approach and the methodological consistency between the data that the atlas was based on and the HCP data that the atlas will be applied to, this is the recommended starting point for cortical network analyses.

2. *Schaefer*

The Schaefer atlas attempts to subdivide the 7 Yeo resting-state subnetworks into functional subregions, using functional connectivity patterns from resting-state and task-based fMRI data and corroboration by histological data (Schaefer et al., 2018). The advantages of the Schaefer atlas are that it was created in surface space and that it can be downloaded in resolutions ranging from 100-1000 regions – making it an excellent atlas for replication of results in different resolutions. The current project includes the parcellation of the HCP-Aging data at low resolution (100 regions), medium resolution (400 regions), and high resolution (1000 regions).

3. *Gordon*

The Gordon atlas takes a similar approach to the Schaefer atlas (using transitions in functional connectivity patterns to define functional region borders), using only resting-state connectivity (Gordon et al., 2016). Due to the fact that the atlas construction took place using a smaller dataset than the other atlases (n=108) and did not employ multimodal strategies such as the Glasser or Schaefer atlas, this atlas may not necessarily be the best starting point for HCP analyses. However, it remains a good-quality atlas (that was constructed using a surface-based approach) for validation purposes of results found in other atlases.

4. *Brainnetome*

The Brainnetome (BNA) atlas subdivides the cortex into 210 regions using machine-learning approaches based on anatomical (DTI) and functional (rs-fMRI) connectivity patterns (Fan et al., 2016). Though the multimodal nature of the BNA atlas is definitely an advantage, the volume-based analysis used in the atlas construction and the small sample size (40 subjects) used for the atlas construction somewhat limit its applicability to HCP data. Nevertheless, as the BNA is widely used

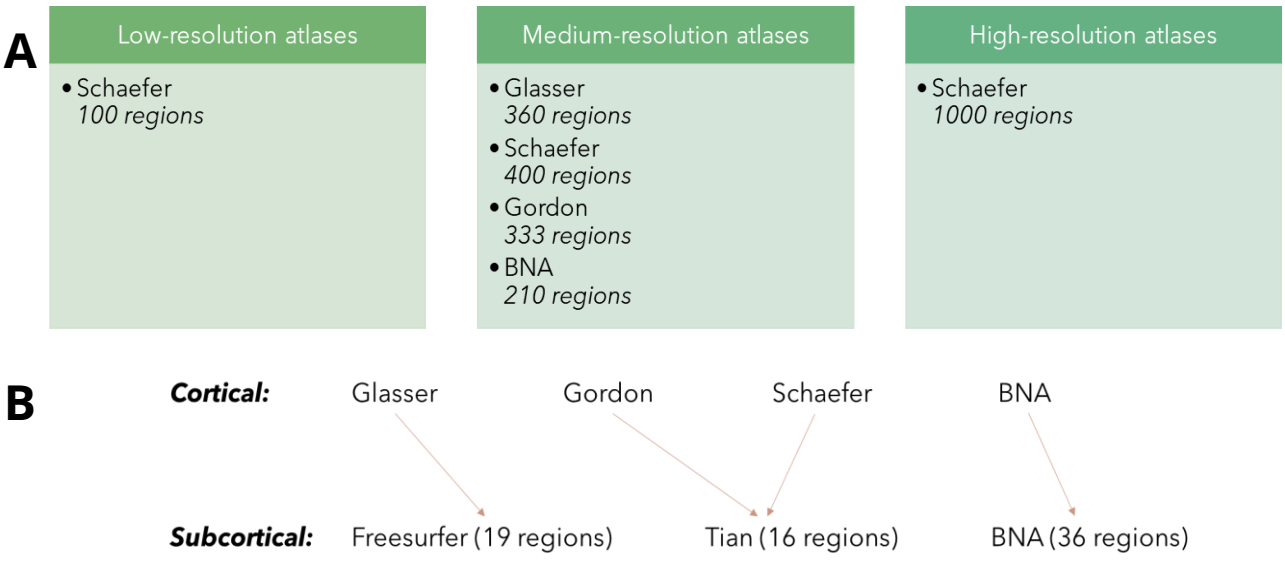

Figure 2: (A) The different types of cortical atlases used for parcellation in this project. (B) The cortical-subcortical atlas matching used in this project.

in non-HCP fMRI studies, it is relevant to include this atlas in the current project as it can be used to easily validate and compare results from this dataset with results from other studies.

Atlas Selection – Subcortex

1. *Freesurfer*

The Freesurfer software provides the option to automatically segment several subcortical structures. Helped by the fact that much of the HCP preprocessing pipelines use Freesurfer, the HCP creators recommend adding the standard Freesurfer subcortical segmentation atlas to the Glasser cortical atlas. Using the Glasser+Freesurfer combination therefore seems like a sensible 'standard' atlas choice.

2. *Tian*

The Freesurfer atlas is based on segmentation on structural images but does not have anything to do with functional connectivity patterns. Using a well-validated subcortical atlas based on functional connectivity therefore seemed necessary for use with the other cortical atlases. The Tian atlas is a recent subcortical atlas based on high-quantity and high-quality functional data (Tian et al., 2020). Tian et al. themselves propose using this atlas in combination with cortical atlases such as the Schaefer and Gordon atlas, which is why this subcortical atlas was chosen to accompany these cortical atlases.

3. *Brainnetome*

The Brainnetome cortical parcellation is accompanied by a subcortical parcellation consisting of 36 subregions.

Zenodo/Github file organization

The connectivity matrices for all subjects (and all atlases) in the two databases are publicly available as a Zenodo dataset.

The Github repository provides all the scripts and files that are necessary to create the parcellated time series and connectivity matrices for the different atlases. The structure of the repository is as follows:

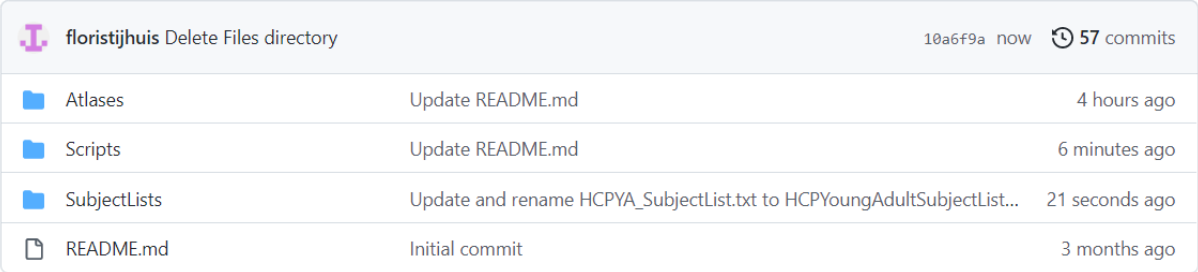

Figure 3: The structure of the Github repository related to the current project

- The /Atlases folder contains the constructed brain atlases in CIFTI format and instructions on how to download and create these final atlases from files available online.
- The /Scripts folder contains two different types of scripts; the scripts that were necessary to generate the atlases (COGparcelsGlasser.sh and bna_atlas_correct_numbering_vertices.m) and the scripts that were used to perform all the processing steps (i.e. downloading preprocessing, and parcellating) on the scans (rsfMRI_Download_Normalization_Concatenation_Parcellation_HCPAging.sh and rsfMRI_Download_Normalization_Concatenation_Parcellation_HCPYoungAdult.sh). If you run these processing scripts, the file structure of a single subject will be structured

in the way that is shown in Figure 4.[3] Each line of the *timeseries.txt* file describes the BOLD signal of 1 brain region at different time points. The connectivity matrices were obtained by calculating a Pearson correlation coefficient between the functional time series describing the activity of the different brain regions. As such, these files are *n*×*n* matrices containing correlation coefficients between each pair of brain regions (in which *n* describes the number of brain regions). In order to see which line corresponds to which brain region, please refer to the annotation files in the /Atlases folder.

- The /SubjectLists folder has one .txt file for each database containing the subject ID's the script uses to loop over. These may be altered in order to only analyze a subset of subjects (this is easily doable for the HCP-Young Adult using db.connectome.org) or to process a new batch of subjects (e.g. when additional HCP-Aging data are released).

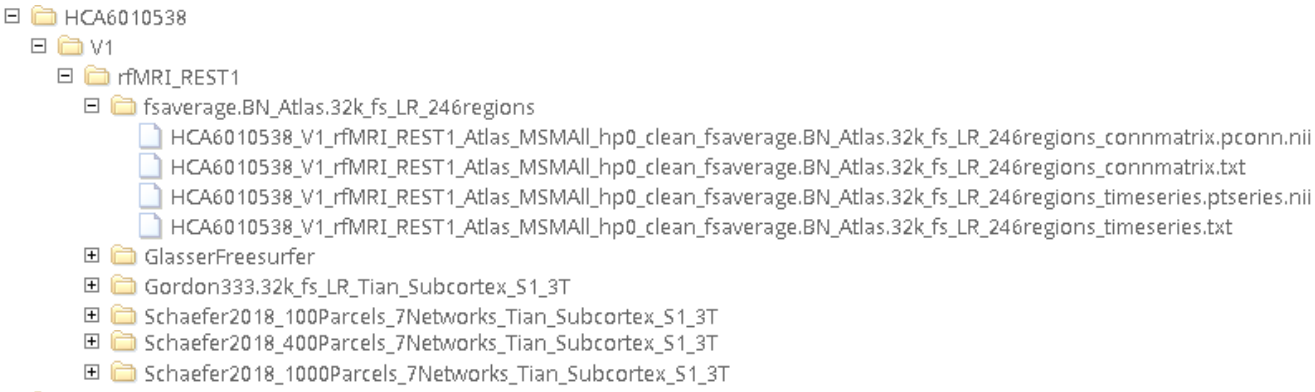

Figure 4: The folder structure for a HCP-Aging subject after running the script, containing the time series and connectivity matrix both in CIFTI format and as a .txt file. The structure for the HCP-Young Adult database is practically the same, except for the fact that the 'V1' folder does not exist in the Young Adult database (as it is a cross-sectional dataset, there will be no 'V2' for subjects in that database).

Future steps

There are several ways to use the scripts and files provided in this repository for your own research purposes. For inspiration and guidance, see some ideas below:

New data releases

The HCP-Young Adult database has finished data collection, so no new data will become available. Though the current release of the HCP-Aging database contains cross-sectional data of 725 subjects, more data is expected later (the first data potentially coming as early as late 2022). The ultimate goal is to include >1500 subjects with >600 subjects having longitudinal measurements. When new data releases become available, it is easy to alter the existing scripts to be able to add these data to the already existing data after processing. For more information, see the comments in the scripts in the GitHub repository.

Task-based fMRI analysis

Whereas the current goal was to process resting-state fMRI data, the scripts can be adapted easily to be used for network analysis of task data as well. Some factors to take into account when pursuing this:

- The current scripts will yield time series for the entire task, regardless of the timing of the task cues. In case you want to perform analyses that take into account the temporal structure of the task (e.g. instructions, tasks, or movements), this needs to be accounted

[3] Privacy and storage limitations made publishing of the entire time series in this public repository not possible.

for. Alternatively, it is possible to perform network analysis on the functional connectivity during the entire task.

- As the task-data was only acquired in one phase-encoding direction, the demeaning and variance normalization performed for the rs-fMRI analysis is not necessary. Rather, the downloaded 'minimally preprocessed' files can be parcellated directly. Note that these steps may still be required if you want to compare the results with resting-state results that did perform these processing steps, or if you want to concatenate task data and resting-state data to create one time series for all the fMRI data. In conclusion, it will require some adaptation of the scripts provided here.

New atlases

It may be possible that you want to parcellate the HCP data using different atlases than the ones provided here or a different cortical/subcortical atlas combination. As long as you have a correct atlas in the CIFTI format (as a .dlabel.nii file), this is easily implemented in the existing scripts. Using the wb_view software, you can easily check to see if the atlas is correct (e.g. whether it has full coverage of all the vertices in the brain). Atlases can either be directly downloadable in the CIFTI format, or can be generated and modified from NIFTI atlases (it is possible to use wb_command for such purposes). Yet, it is important to realize that using an atlas intended for use in volume space will yield suboptimal registration results and may negate (some of the) benefits that arise from using high-quality HCP data.

Multiscale explanations

In addition to fMRI data, the HCP protocol collects various different types of data that may be combined with fMRI data. In terms of neuroimaging data, both datasets include structural connectivity measured using diffusion tensor imaging (DTI) and a subset of HCP-Young Adult subjects also underwent MEG. Behaviorally, a cognitive and performance battery is administered in order to assess cognitive and physical fitness. Lastly, a wide variety of biomarkers is obtained for each subject in the HCP-Aging database (less so for the HCP-Young Adult database), including information on hormonal, metabolic, genotypic, and environmental characteristics. For a full explanation on which non-fMRI data is present in both databases, please refer to (Elam et al., 2021) for the HCP-Young Adult database and (Bookheimer et al., 2019) for the HCP-Aging database.

Combining these different data types with the resting-state fMRI data presented here allows correlating brain connectivity to these metrics as well as the development of multiscale frameworks and/or multilayer brain networks. In order to use the behavioral data collected by the HCP, you need to have access to the database (explained in the *Databases* section above) and download it from there. For the HCP-Aging, you can use the download instructions to create and download the data package containing the behavioral data (HCPAgingImgManifestBeh). For the HCP-Young Adult database, you can log in to Connectome DB to download a spreadsheet with the behavioral data.

References

Bookheimer, S. Y., Salat, D. H., Terpstra, M., Ances, B. M., Barch, M., Buckner, R. L., Burgess, G. C., Curtiss, S. W., Diaz-, M., Elam, J. S., Fischl, B., Greve, D. N., Hagy, H. A., Harms, M. P., Hatch, O. M., Hedden, T., Hodge, C., Japardi, K. C., Kuhn, T. P., … Angeles, L. (2019). The Lifespan Human Connectome Project in Aging: An overview. *NeuroImage*, *185*, 335–348. https://doi.org/10.1016/j.neuroimage.2018.10.009

Brodoehl, S., Gaser, C., Dahnke, R., Witte, O. W., & Klingner, C. M. (2020). Surface-based analysis increases the specificity of cortical activation patterns and connectivity results. *Scientific Reports*, *10*(1), 5737. https://doi.org/10.1038/s41598-020-62832-z

Coalson, T. S., van Essen, D. C., & Glasser, M. F. (2018). The impact of traditional neuroimaging methods on the spatial localization of cortical areas. *Proceedings of the National Academy of Sciences of the United States of America*, *115*(27), E6356–E6365. https://doi.org/10.1073/pnas.1801582115

Elam, J. S., Glasser, M. F., Harms, M. P., Sotiropoulos, S. N., Andersson, J. L. R., Burgess, G. C., Curtiss, S. W., Oostenveld, R., Larson-Prior, L. J., Schoffelen, J. M., Hodge, M. R., Cler, E. A., Marcus, D. M., Barch, D. M., Yacoub, E., Smith, S. M., Ugurbil, K., & van Essen, D. C. (2021). The Human Connectome Project: A retrospective. *NeuroImage*, *244*(August), 118543. https://doi.org/10.1016/j.neuroimage.2021.118543

Fan, L., Li, H., Zhuo, J., Zhang, Y., Wang, J., Chen, L., Yang, Z., Chu, C., Xie, S., Laird, A. R., Fox, P. T., Eickhoff, S. B., Yu, C., & Jiang, T. (2016). The Human Brainnetome Atlas: A New Brain Atlas Based on Connectional Architecture. *Cerebral Cortex*, *26*(8), 3508–3526. https://doi.org/10.1093/cercor/bhw157

Glasser, M. F., Coalson, T. S., Robinson, E. C., Hacker, C. D., Yacoub, E., Ugurbil, K., Andersson, J., Beckmann, C. F., Jenkinson, M., Smith, S. M., & Essen, D. C. van. (2017). A multi-modal parcellation of human cerebral cortex. *Nature*, *536*(7615), 171–178. https://doi.org/10.1038/nature18933

Glasser, M. F., Sotiropoulos, S. N., Wilson, J. A., Coalson, T. S., Fischl, B., Andersson, J. L., Xu, J., Jbabdi, S., Webster, M., Polimeni, J. R., van Essen, D. C., & Jenkinson, M. (2013). The Minimal Preprocessing Pipelines for the Human Connectome Project and for the WU-Minn HCP Consortium. *Neuroimage*, *80*, 105–12404. https://doi.org/10.1016/j.neuroimage.2013.04.127

Gordon, E. M., Laumann, T. O., Adeyemo, B., Huckins, J. F., Kelley, W. M., & Petersen, S. E. (2016). Generation and Evaluation of a Cortical Area Parcellation from Resting-State Correlations. *Cerebral Cortex*, *26*(1), 288–303. https://doi.org/10.1093/cercor/bhu239

Harms, M. P., Somerville, L. H., Ances, B. M., Andersson, J., Barch, D. M., Bastiani, M., Bookheimer, S. Y., Brown, T. B., Buckner, R. L., Burgess, G. C., Coalson, T. S., Chappell, M. A., Dapretto, M., Douaud, G., Fischl, B., Glasser, M. F., Greve, D. N., Hodge, C., Jamison, K. W., … Yacoub, E. (2018). Extending the Human Connectome Project across ages: Imaging protocols for the Lifespan Development and Aging projects. *NeuroImage*, *183*, 972–984. https://doi.org/10.1016/j.neuroimage.2018.09.060

Robinson, E. C., Garcia, K., Glasser, M. F., Chen, Z., Coalson, S., Makropoulos, A., Bozek, J., Wright, R., Schuh, A., Webster, M., Hutter, J., Price, A., Grande, L. C., Hughes, E., Tusor, N., Bayly, P. v, Essen, D. C. van, Smith, S. M., Edwards, A. D., … Kingdom, U. (2018). Multimodal Surface

Matching with Higher-Order Smoothness Constraints. *NeuroImage*, *167*, 453–465. https://doi.org/10.1016/j.neuroimage.2017.10.037

Schaefer, A., Kong, R., Gordon, E. M., Laumann, T. O., Zuo, X.-N., Holmes, A. J., Eickhoff, S. B., & Yeo, B. T. T. (2018). Local-Global Parcellation of the Human Cerebral Cortex from Intrinsic Functional Connectivity MRI. *Cerebral Cortex*, *28*(9), 3095–3114. https://doi.org/10.1093/cercor/bhx179

Smith, S. M., Beckmann, C. F., Andersson, J., Auerbach, E. J., Bijsterbosch, J., Douaud, G., Duff, E., Feinberg, D. A., Griffanti, L., Harms, M. P., Kelly, M., Laumann, T., Miller, K. L., Moeller, S., Petersen, S., Power, J., Salimi-Khorshidi, G., Snyder, A. Z., Vu, A. T., … Glasser, M. F. (2013). Resting-state fMRI in the Human Connectome Project. *NeuroImage*, *80*, 144–168. https://doi.org/10.1016/j.neuroimage.2013.05.039

Tian, Y., Margulies, D. S., Breakspear, M., & Zalesky, A. (2020). Topographic organization of the human subcortex unveiled with functional connectivity gradients. *Nature Neuroscience*, *23*(11), 1421–1432. https://doi.org/10.1038/s41593-020-00711-6

van Essen, D. C., Smith, S. M., Barch, D. M., Behrens, T. E. J., Yacoub, E., & Ugurbil, K. (2013). The WU-Minn Human Connectome Project: An overview. *NeuroImage*, *80*, 62–79. https://doi.org/10.1016/j.neuroimage.2013.05.041

Appendix 1: Boilerplate text describing rfMRI processing

HCP Young Adult

The data used here were taken from the Human Connectome Project (HCP) Young Adult database. For a full description of this database, please refer to (van Essen et al., 2013). Here, a description of the image acquisition and processing protocols is given.

The resting-state fMRI data were collected on a 3T Skyra (Siemens) scanner using a 32-channel head coil. Two resting-state functional MRI scans (eyes open, focusing on a white cross) were performed, with each of the resting-state scans consisting of two 14-minute discontinuous subscans acquired in opposite phase encoding directions (L/R and R/L). Each of the subscans consisted of 2400 volumes of echo planar images (2x2x2 mm isotropic resolution, TR/TE = 720/33 ms, flip angle = 52°) (Smith et al., 2013).

HCP Aging

The data used here were taken from the Human Connectome Project (HCP) Aging database. For a full description of this database, please refer to (Bookheimer et al., 2019). Here, a description of the image acquisition and processing protocols is given.

The resting-state fMRI data were collected on a 3T Siemens Prisma scanner using a 32-channel head coil. Two resting-state functional MRI scans (eyes open, focusing on a white cross) were performed, with each of the resting-state scans consisting of two 6.5-minute discontinuous subscans acquired in opposite phase encoding directions (A/P and P/A). Each of the subscans consisted of 488 volumes of echo planar images (2x2x2 mm isotropic resolution, TR/TE = 800/37 ms, flip angle = 52°) (Harms et al., 2018).

Final part – applicable to both HCP-YA and HCP-Aging

Each of these subscans were first processed according to the standard minimal preprocessing pipeline recommended by the HCP creators (Glasser et al., 2013). Briefly, the *fMRIVolume* pipeline performs some basic preprocessing steps on the raw fMRI scan in volume space, including gradient nonlinearity distortion correction, head motion parameter frame realignment, susceptibility distortion correction and registration to MNI space, after which intensity normalization (mean intensity of 10000) and brain masking is performed. *fMRISurface* maps the activity from volume space to the cortical surface and performs 2mm Gaussian smoothing on the surface. After this, *ICA-FIX* was used to remove (motion) artefacts and noise in the data (using surface-based data). Lastly, the *MSMAII* pipeline was employed, align the individual functional scan to a group template using a multimodal approach (Robinson et al., 2018).

Next, custom scripts were used to finalize preprocessing and obtain the parcellated time series for the two resting state scans, following recommendations provided on the HCP website (ZENODO). First, the two subscans were normalized using demeaning and variance normalization, after which they were concatenated. Next, each of the resting-state scans was parcellated using the **[INSERT ATLAS]**. The grayordinate signal in each brain region in the brain atlas was averaged and extracted, yielding a time series describing the BOLD activity of these brain regions over time. Lastly, an $n \times n^4$ functional connectivity matrix was created by calculating the Pearson correlation coefficient of the functional time series of each pair of brain regions.

[4] Insert the number of brain regions your chosen atlas contains here.