**IMAGEN Resting-State Processing Pipeline:**

1. QC steps on raw data:
2. Identification movement and slice artifacts (using FSL and ArtRepair routines) – custom Matlab scripts (**QC\_pipeline.m**; **save\_QC\_output.m**; **cell2csv.m**).   
     
   Files generated: **QC\_Table\_BL.csv** & **QC\_Table\_FU2.csv**
   * 1. Most important are the columns: Max FD > criterion (i.e., 0.5), Mean FD, Max movement (rotations and translations) in three directions, Artifact slice percent. Note that the latter can sometimes be really high because of extremely high values within as compared to outside the brain. This does not pose a problem. Always check whether slice artifacts are visible in the datasets.
3. Creation of temporal standard deviation (tstd) and temporal signal-to-noise (tsnr = temporal mean / tstd) for identification of acquisition artifacts. FSL command line tool **fslmaths** used with -Tmean, -Tstd, and -div options. Folders generated:

Folders generated: **TSNR\_images\_BL** & **TSNR\_images\_FU2**

Subfolders: **slicesdir\_tstd\_BL** & **slicesdir\_tstd\_FU2**

**slicesdir\_tsnr\_BL** & **slicesdir\_tsnr\_FU2**

(html report pages to view: **index.html**)

1. Preprocessing of raw data:
2. Motion correction (FSL **MCFLIRT**), skull stripping (FSL **BET**), spatial smoothing (4mm FWHM) within FSL **FEAT**, and grand mean intensity normalization (each volume is scaled by the same amount). Note that the rest of the preprocessing pipeline was done on both smoothed and unsmoothed images.

Files generated: **example\_design\_file\_smooth.fsf**

**example\_design\_file\_nonsmooth.fsf**

Contains the preprocessing parameters; can be viewed in text editor or loaded into the Feat GUI.

Folders generated: **Motion\_BL**

**Motion\_FU2**

Containing the FD and six motion parameters files

1. Calculation of registration parameters of EPI (unsmoothed) to T1 (FSL **FLIRT**, using the linear Boundary Based Registration [**BBR**] algorithm), and T1 to 2mm MNI standard space (nonlinear registration; **ANTS**) – custom shell script (**registration\_IMAGEN.sh**; requires FSL and ANTS to be installed)

Folders generated: **Registrations\_BL/<code>/reg Registrations\_FU2/<code>/reg**

Containing the registration matrices and warp images that can be used with FLIRT and ANTS.

Files generated: **slicesdir\_BL\_registrations**

**slicesdir\_FU2\_registrations**

(html report pages to view: **index.html**; triplets of images: epi to mni [1st row], epi to T1 [2nd row], T1 to mni [3rd row]; the red outline always displays the registered image, the target is the underlying image).

1. ICA–based artifact filtering using ICA-AROMA – slightly adapted version of ICA\_AROMA python scripts (**ICA\_AROMA\_IMAGEN.py**; **ICA\_AROMA\_\_IMAGEN\_functions.py**; **ICA\_AROMA\_IMAGEN\_functions.pyc**; requires the T1 \_brain image to be saved in the reg folder of the individuals’ FEAT directory).  
     
   Folder with functions and other files: **ICA\_AROMA\_IMAGEN**
2. Detrending (1st - 3rd order) of artifact-filtered data – custom python function (**DETREND.PY**)
3. Preprocessed data sets registered to 2mm MNI standard space, using the registration parameters obtained at step 2b and resliced to 3mm isotropic voxels.
4. Final preprocessed data sets are stored.

Folders generated: **Preprocessed\_data**

Files generated: **<code>\_preproc\_smooth.nii.gz**

**<code>\_preproc\_nonsmooth.nii.gz**

**<code>\_preproc\_smooth.nii.gz**

**<code>\_preproc\_nonsmooth.nii.gz**

Folders generated: **TSNR\_images\_preproc\_BL**

**TSNR\_images\_preproc\_FU2**

Subfolders: **slicesdir\_tstd\_BL\_(non)smooth**

**slicesdir\_tstd\_FU2\_(non)smooth**

**slicesdir\_tsnr\_BL\_(non)smooth**

**slicesdir\_tsnr\_FU2\_(non)smooth**

(html report pages to view: **index.html**)

Can be used to view the impact of preprocessing and for final visual artifact identification.

**Preprocessing text for Methods section:**

Preprocessing of resting-state data was performed with routines from FMRIB’s Software Library (FSL v5.0.9) and Advanced Normalization Tools (ANTs v1.9.2). 1) Motion correction was carried out, applying a rigid body registration of each volume to the middle volume (FSL MCFLIRT). 2) Non-brain tissue was removed (FSL BET). [optional: 3) Spatial smoothing was applied using a 4mm FWHM Gaussian kernel]. 4) Independent component analysis (FSL MELODIC) was run for each data set. Artifact components were identified using an automatic classification algorithm, and subsequently regressed from the data (ICA-AROMA v0.3; Pruim et al., 2015). 5) The resulting cleaned data set was detrended (up to a third degree polynomial). 6) Coregistration to a high-resolution T1 image (FSL FLIRT using the BBR algorithm), and normalization to 2mm isotropic MNI standard space (ANTs) was carried out. 7) Lastly, preprocessed and normalized resting-state data sets were resliced to 3mm isotropic voxels.

**Reference**

Pruim RH, Mennes M, van Rooij D, Llera A, Buitelaar JK, Beckmann CF (2015). ICA-AROMA: A robust ICA-based strategy for removing motion artifacts from fMRI data. *Neuroimage*, *112*, 267-277.

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Charité Universitätsmedizin Berlin, Department of Psychiatry and Psychotherapy, Berlin, Germany

\* For questions related to the preprocessing of the IMAGEN resting-state data, please contact Dr. Ilya Veer: [ilya.veer@charite.de](mailto:ilya.veer@charite.de)