

DOCUMENTATION

of

BRAIN MEASURES

in

MIDUS Refresher 1

Neuroscience Project (P5)

University of Wisconsin ♦ Institute on Aging
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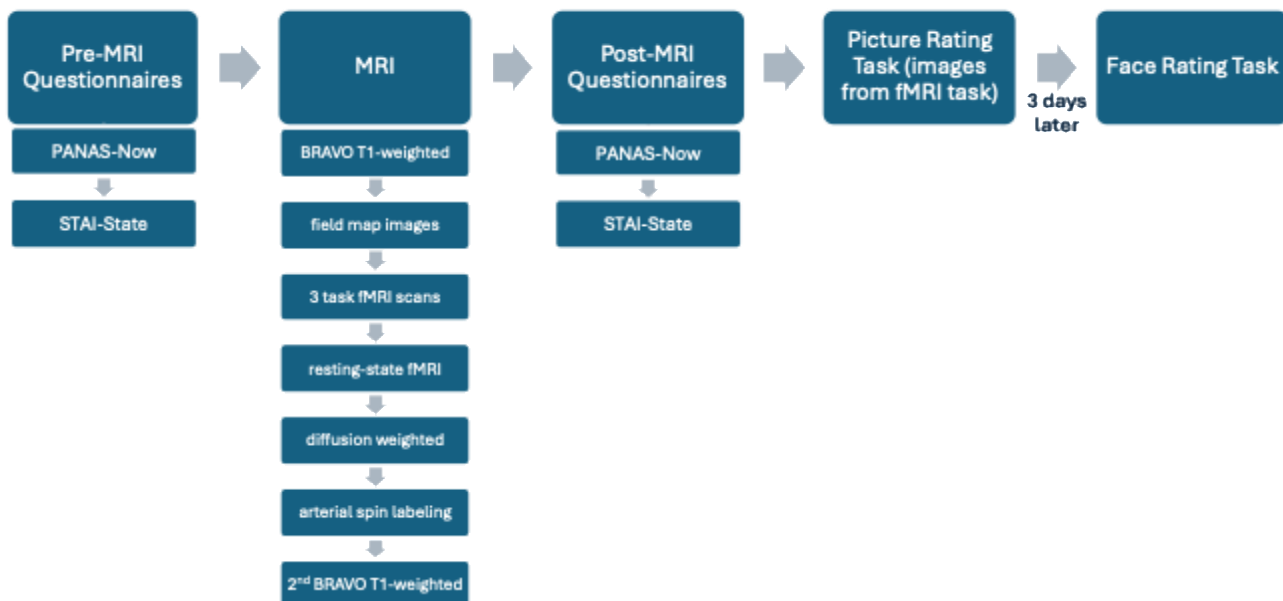
INTRODUCTION

This document is an updated reference for the extracted structural and diffusion brain measures and metrics derived from brain-based aging algorithms from the MIDUS Refresher 1 Neuroscience Project data set. This document also includes information regarding the Neuroscience Project's (P5) MIDUS Refresher 1 MRI data collection and processing protocols.

Raw MRI data (including structural, task functional, resting functional, diffusion-weighted imaging, and resting perfusion) and associated behavioral data are available through a restricted access data sharing mechanism. Please see *MR1_P5_RESTRICTED_ACCESS_20260106* and/or <https://midus.wisc.edu/midus-neuroscience-repository/> for more information about what is available and instructions on how to access these data.

General information about MRI scans

All MIDUS Refresher 1 scans were performed at the Waisman Brain Imaging Laboratory on the UW-Madison campus using a 3T MR750 GE Healthcare MRI scanner (Waukesha, WI) and an 8-channel head coil. MRI scans typically took place during the morning of the second day of Neuroscience Project data collection (see **RA5ITS** and **RA5ITF** for the exact MRI start times). In total, the scanning protocol had a duration of approximately 70 minutes and included the acquisition of a BRAVO T1-weighted scan, field map images, 3 task functional MRI (fMRI) scans/EPIs, a resting-state fMRI scan, a diffusion-weighted scan, an arterial spin labeling scan, as well as a second BRAVO T1-weighted scan when circumstances allowed. Questionnaire data, including PANAS-NOW and STAI-State, both prior to and after the scanning procedure, are also available (see *MR1_P5_DOCUMENTATION_OF_PROCEDURES_20260206* and *MR1_P5_DOCUMENTATION_OF_SCALES_20260206* for more information).



Partial variable names have been provided where appropriate. In partial variable names note that “_” represents a single character. For more detailed information on variable names see variable naming or atlas tables below or see *MR1_P5_VARIABLE_NAMES_20260206*.

Differences Between MIDUS Waves

To aid in the comparison of data described in this document between waves, a brief description of the major differences across waves has been provided.

MIDUS 2 vs MIDUS Refresher 1

The Waisman Brain Imaging MRI scanner was updated between the MIDUS 2 and MIDUS Refresher 1 data collections. Due to limitations in scan quality at the time of MIDUS 2 data collection (which suffered a severe intensity bias that so far has not been able to be corrected with bias corrections), the MIDUS 2 structural data was of insufficient quality to provide these estimates from the structural MRI data. Additionally, diffusion-weighted scanning was not performed at MIDUS 2. Therefore, MIDUS Refresher 1 represents the first instance of the extracted structural and diffusion brain measures and metrics derived from brain-based aging algorithms.

MIDUS 3 vs MIDUS Refresher 1

In MIDUS Refresher 1 an 8-channel head coil was used, but in MIDUS 3 it was swapped for a 32-channel NOVA head coil.

The diffusion-weighted imaging (DWI) acquisitions differed between MIDUS Refresher 1 and MIDUS 3 data collections. Although both MIDUS Refresher 1 and MIDUS 3 have multi-shell DWI data and have extracted diffusion tensor estimates (DTI: FA, MD, AD, RD), those measures should not be combined across MIDUS Refresher 1 and MIDUS 3 without appropriate harmonization of the data. Moreover, the higher diffusion weighting in MIDUS 3 DWI acquisition allowed additional models (DKI, WMTI, NODDI) and their estimates to be computed and extracted.

Scan Data Quality Filters

Most participants who completed the Neuroscience Psychophysiology protocol completed the MRI protocol. In some cases, data could not be collected due to claustrophobia, back problems, or other issues that prevented the participant from completing the MRI scan. A filter variable is provided, indicating whether participants completed a T1-weighted scan **[RA5IC]**. However, a small number of scans contained artifacts that made accurate structural measurements unfeasible. In all cases, the appropriate missing value was listed. A second filter indicates whether a radiologist flagged the scan for an abnormality during review **[RA5IF]**. Radiologist flags were most typically indicating small vessel ischemic disease, presence of meningiomas or other masses, and/or referrals to specialists. Please note that the radiologist only flagged scans with unexpected findings. If a participant self-reported a health concern that could explain an otherwise unusual scan, the scan would not be flagged by the radiologist. For example, the radiologist would have taken into account any self-reported neurological condition as well as other self-reported chronic medical conditions such as diabetes, asthma, hypertension, cancer, and other diseases not listed here which could have affected the brain in ways expected for those conditions typically indicative of accelerated brain aging. During the screening process, participants who self-reported neurological or other health conditions that could impact their data were excluded from the MIDUS Refresher 1 (MR1) Neuroscience project. However, in future waves, to maximize longitudinal data collection, participants were not excluded due to neurological or other health conditions. Therefore, an additional variable of self-reported neurological condition has been provided **[RA5IN]**. The self-reported neurological conditions may include seizure disorders, Parkinson's, tremors, multiple sclerosis, Alzheimer's disease or related dementia, previous stroke/TIA, brain aneurysm, head/brain injury, cyst on the brain, or other condition (unclear if central or peripheral

nervous system condition). Note that because MR1 participants were excluded if they reported a neurological condition, all MR1 participants have a value of 0 for RA5IN.

FREESURFER-EXTRACTED STRUCTURAL BRAIN MEASUREMENTS

Scanning parameters: BRAVO T1-weighted (T1w) structural images with 1 mm³ isotropic voxels (TR = 8.2 ms, TE = 3.2 ms, flip angle = 12°, FOV = 256 mm, 256 x 256 matrix, 156 axial slices, inversion time = 450 ms, total duration = 7.5 minutes).

FreeSurfer processing: For participants with two artifact-free T1-weighted scans, the data from both were averaged during processing with FreeSurfer (v5.3.0). In cases where one of the two scans contained significant artifact or noise, the best available scan was used. Likewise, only one scan was used in processing data from participants for whom a second T1-weighted scan was not collected. Cortical reconstruction and volumetric segmentation was performed with the FreeSurfer image analysis suite (v5.3.0), which is documented and freely available for download online (<http://surfer.nmr.mgh.harvard.edu/>). The technical details of these procedures are described in prior publications (Dale et al., 1999; Dale & Sereno, 1993; Fischl & Dale, 2000; Fischl et al., 2001; Fischl et al., 2002; Fischl et al., 2004a; Fischl et al., 1999a; Fischl et al., 1999b; Fischl et al., 2004b; Han et al., 2006; Jovicich et al., 2006; Segonne et al., 2004; Reuter et al., 2010; Reuter et al., 2012).

Briefly, this processing includes motion correction and averaging (Reuter et al. 2010) of multiple volumetric T1-weighted images (when more than one is available), removal of non-brain tissue using a hybrid watershed/surface deformation procedure (Segonne et al., 2004), automated Talairach transformation, segmentation of the subcortical white matter and deep gray matter volumetric structures (including hippocampus, amygdala, caudate, putamen, ventricles) (Fischl et al., 2002; Fischl et al., 2004a) intensity normalization (Sled et al., 1998), tessellation of the gray matter white matter boundary, automated topology correction (Fischl et al., 2001; Segonne et al., 2007), and surface deformation following intensity gradients to optimally place the gray/white and gray/cerebrospinal fluid borders at the location where the greatest shift in intensity defines the transition to the other tissue class (Dale et al., 1999; Dale & Sereno, 1993; Fischl & Dale, 2000). Once the cortical models are complete, a number of deformable procedures can be performed for further data processing and analysis including surface inflation (Fischl et al., 1999a), registration to a spherical atlas which is based on individual cortical folding patterns to match cortical geometry across subjects (Fischl et al., 1999b), parcellation of the cerebral cortex into units with respect to gyral and sulcal structure (Desikan et al., 2006; Fischl et al., 2004b; Klein & Tourville, 2012), and creation of a variety of surface based data including maps of curvature and sulcal depth. This method uses both intensity and continuity information from the entire three-dimensional MR volume in segmentation and deformation procedures to produce representations of cortical thickness, calculated as the closest distance from the gray/white boundary to the gray/CSF boundary at each vertex on the tessellated surface (Fischl & Dale, 2000). The maps are created using spatial intensity gradients across tissue classes and are therefore not simply reliant on absolute signal intensity. The maps produced are not restricted to the voxel resolution of the original data thus are capable of detecting submillimeter differences between groups. Procedures for the measurement of cortical thickness have been validated against histological analysis (Rosas et al., 2002) and manual measurements (Kuperberg et al., 2003; Salat et al., 2004). FreeSurfer morphometric procedures have been demonstrated to show good test-retest reliability across scanner manufacturers and across field

strengths (Han et al., 2006; Reuter et al., 2012). Segmentation quality was visually assessed and manually edited as necessary (<http://freesurfer.net/fswiki/Edits>). After the manual edits segmentation of the hippocampal subfields and amygdala nuclei was performed using developmental version in FreeSurfer v6.0.0. Description of these segmentations can be found in Iglesias et al. (2015) for the hippocampus and Saygin and Kliemann et al. (2017) for the amygdala.

Extracted FreeSurfer measures are provided for 127 participants

- Using FreeSurfer (v5.3.0) cortical parcellation was performed using 3 atlases to calculate measures of cortical thickness, curvature, surface area, and volume:
 - Destrieux atlas (Fischl et al., 2004b) [RA5E__D...]
 - Desikan-Killiany atlas (Desikan et al., 2006) [RA5E__K...]
 - Desikan-Killiany-Tourville (DKT) atlas (Klein & Tourville, 2012) [RA5E__T...]
- Subcortical volumes [RA5ES_A...] were derived via the
 - Automatic Segmentation (aseg) atlas (Fischl et al., 2002) – using FreeSurfer v5.3.0
 - Hippocampal and Amygdala segmentation modules performed using FreeSurfer v6.0.0
 - Hippocampal subfields (Iglesias et al., 2015)
 - Nuclei of the amygdala (Saygin & Kliemann et al., 2017)

Differences in FreeSurfer naming conventions between waves: For the MIDUS Refresher 1 wave, an aseg variable labeled as ‘CorticalWhiteMatter’ was extracted using FreeSurfer v5.3.0. For MIDUS 3, FreeSurfer v6.0.0 re-labeled that same aseg variable as ‘CerebralWhiteMatter’. FreeSurfer creators thought ‘CerebralWhiteMatter’ was the better naming convention, but these variables reflect the same measure across waves.

BRAIN-BASED AGING ALGORITHMS

Scanning parameters: BRAVO T1-weighted (T1w) structural images with 1 mm³ isotropic voxels (TR = 8.2 ms, TE = 3.2 ms, flip angle = 12°, FOV = 256 mm, 256 x 256 matrix, 156 axial slices, inversion time = 450 ms, total duration = 7.5 minutes).

Dunedin Pace of Aging Calculated from NeuroImaging (DunedinPACNI)

The DunedinPACNI is a computed measure of “the rate of longitudinal aging” derived from cross-sectional brain magnetic resonance imaging (Whitman et al., 2025).

Processing for DunedinPACNI: The output of the FreeSurfer parcellations was also used to derive the Dunedin Pace of Aging Calculated from NeuroImaging (DunedinPACNI) [RA5EBD]. We ran the open source DunedinPACNI package at HEAD, commit 3760130 on T1-weighted MRI scans that were preprocessed and parcellated using FreeSurfer image analysis suite (v6.0.0). See the DunedinPACNI documentation for detailed information about the algorithm.

Whitman, E. T., Elliott, M. L., Knodt, A. R., Abraham, W. C., Anderson, T. J., Cutfield, N. J., Hogan, S., Ireland, D., Melzer, T. R., Ramrakha, S., Sugden, K., Theodore, R., Williams, B. S., Caspi, A., Moffitt, T. E., & Hariri, A. R. (2025). DunedinPACNI estimates the longitudinal Pace of Aging from a single brain image to track health and disease. *Nature aging*, 5(8), 1619–1636. <https://doi.org/10.1038/s43587-025-00897-z> PMID: 40595015

GitHub link: <https://github.com/etw11/DunedinPACNI>

Brain-Predicted Age

Brain-predicted age was calculated using multiple publicly shared algorithms and deep learning models which have been pretrained with cross-validation on other external T1-weighted MRI datasets:

Cole Brainage Estimates

Cole brainageR v1.0 [RA5EB] and Cole brainageR v2.0 [RA5EBC] both using Gaussian Processes regression described in detail on <https://github.com/james-cole/brainageR>, which according to the GitHub description use similar but not identical methods as Cole, J. H., Leech, R., Sharp, D. J., & Initiative, A. D. N. (2015). Prediction of brain age suggests accelerated atrophy after traumatic brain injury. *Annals of Neurology*, 77(4), 571–581. doi: 10.1002/ana.24367.

Processing for BrainAgeR v1.0 estimation: The software takes raw T1-weighted MRI scans, then uses SPM12 for segmentation and normalisation. A slightly customized version of FSL's `slicdir*` is then used to generate a directory of PNGs and corresponding index.html file for quality controlling in a web browser. Finally, the normalised images are loaded into R using the `RNfiti` package, vectorised and grey matter, white matter, and CSF vectors masked (using 0.3 in the average image from the brainageR-specific template, derived from n=200 scans, n=20 from each of the n=10 scanners) and combined.

GitHub link - BrainAgeR v1.0: <https://github.com/james-cole/brainageR/tree/1.0>

Processing for BrainAgeR v2.0 estimation: In version 2.0 of Cole's software, Principal Components Analysis was run (using R's `prcomp`), and the top 80% of variance retained. This meant 435 PCs were included. The rotation matrix of the PCA is applied to any new data and these 435 variables are then used to predict an age value with the trained model with `**kernlab**`. The entailed using a GPR with RBF kernel and default hyperparameters.

GitHub link - BrainAgeR v2.0: <https://github.com/james-cole/brainageR/tree/2.0>

Citation information:

The GitHub details for Cole v1.0 and v2.0 include a request for R citation. "Since kernlab does most of the heavy lifting, please consider citing this excellent package:

<https://cran.r-project.org/web/packages/kernlab/citation.html>."

"This model has yet to be used in a publication as of 30/09/2019, however some of the training dataset and general approach have been used before. So if you use this software, please consider citing one or more of the following papers:

Cole JH, Ritchie SJ, Bastin ME, Valdes Hernandez MC, Munoz Maniega S, Royle N et al. Brain age predicts mortality. *Molecular psychiatry* 2018; 23: 1385-1392.

Cole JH, Poudel RPK, Tsagkrasoulis D, Caan MWA, Steves C, Spector TD et al. Predicting brain age with deep learning from raw imaging data results in a reliable and heritable biomarker. *NeuroImage* 2017; 163C: 115-124.

Cole JH, Leech R, Sharp DJ, for the Alzheimer's Disease Neuroimaging Initiative. Prediction of brain age suggests accelerated atrophy after traumatic brain injury. *Ann Neurol* 2015; 77(4): 571-581."

However, it is important to note that none of these papers' methods exactly match the GitHub description, so they provide the gist but not exact details of the methods.

TSAN Brainage Estimates [RA5EBT] - PMID: 34086565

The Two-Stage-Age-Net (TSAN) is an algorithm used to estimate brainage using T1-weighted MRI data.

Processing for TSAN estimation: Raw T1-weighted MRI scans were preprocessed following the guidelines presented in the GitHub repository for TSAN. The data were reoriented to the standard MNI orientation. The images were skull-stripped, and corrected for B1 bias using the N4 algorithm implemented in ANTs. The data were then non-linearly registered to MNI 2 mm x 2 mm x 2 mm MNI skull stripped template. These preprocessed images were fed as input to the trained deep learning model described in these papers:

Cheng, J., Liu, Z., Guan, H., Wu, Z., Zhu, H., Jiang, J., Wen, W., Tao, D., & Liu, T. (2021). Brain Age Estimation From MRI Using Cascade Networks With Ranking Loss. *IEEE transactions on medical imaging*, 40(12), 3400–3412.

<https://doi.org/10.1109/TMI.2021.3085948> PMID: 34086565

Liu, Z., Cheng, J., Zhu, H., Zhang, J., & Liu, T. (2020). Medical Image Computing and Computer Assisted Intervention – MICCAI 2020, 23rd International Conference, Lima, Peru, October 4–8, 2020, Proceedings, Part VII. *Lecture Notes in Computer Science*, 198–207. https://doi.org/10.1007/978-3-030-59728-3_20

GitHub link: TSAN-brain-age-estimation: TSAN: Two-Stage-Age-Net, for brain age estimation from T1-weighted MRI data <https://github.com/Milan-BUAA/TSAN-brain-age-estimation>

3D-CNN Brainage Estimates [RA5EBP] - PMID: 36595679

The three-dimensional convolution neural network (3D-CNN) is an algorithm used to estimate brainage using T1-weighted MRI data.

Processing for 3D-CNN estimation: Raw T1-weighted MRI scans were preprocessed with the FreeSurfer image analysis suite (v6.0.0), and the brain.mgz file output from FreeSurfer were used as input to the trained deep learning model as described in this paper:

Yin, C., Imms, P., Cheng, M., Amgalan, A., Chowdhury, N. F., Massett, R. J., Chaudhari, N. N., Chen, X., Thompson, P. M., Bogdan, P., Irimia, A., & Alzheimer's Disease Neuroimaging Initiative (2023). Anatomically interpretable deep learning of brain age captures domain-specific cognitive impairment. *Proceedings of the National Academy of Sciences of the United States of America*, 120(2), e2214634120.

<https://doi.org/10.1073/pnas.2214634120> PMID: 36595679

GitHub link: https://github.com/irimia-laboratory/USC_BA_estimator

DIFFUSION-WEIGHTED IMAGING (DWI)-BASED MEASUREMENTS

Scanning parameters: A Stejskal-Tanner [J. Chem. Phys. 42, 288 (1965)] diffusion prepared spin echo EPI sequence was used with the following parameters: 65 x 2 mm axial slices, within plane field of view = 256mm x 256 mm, acquisition matrix 128 x 128 (readout R/L), partial Fourier encoding 62.5% and ASSET (SENSE) x 2. Additional parameters TR = 7000 ms; TE = 68.7 – 69.0 ms. Four reference scans ($b=0$ s/mm²) and two concentric shells ($b=400$ s/mm² and $b=1200$ s/mm²) were acquired with 6 and 70 directions respectively.

Image processing: The DWI data were used to extract the diffusion tensor imaging (DTI) (Alexander et al., 2011; Jones & Leemans, 2011; Le Bihan et al., 2001) metrics. The data were denoised using the “dwdenoise” function in MRtrix3 (v. 3.0_RC2, using Eigen 3.2.5). MRtrix3’s “mrdegibbs” function was then applied to the data in order to remove Gibbs ringing artifacts from the images. Next, the “eddy” function in FSL (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/>; v5.0.11) was applied to the data to correct for eddy current-induced distortions and subject movements. Images were then skull-stripped using FSL’s “bet” function and a binary brain mask was created using the skull-stripped data. Using DIPY (<https://nipy.org/dipy/>; v0.14.0), DTI tensors were fit at each voxel using a weighted least squares optimization. After tensors were fitted to the data, each participant’s data was visually inspected for quality assurance purposes. A study-specific population Fractional Anisotropy (FA) template was then created using ANTS (<http://picsl.upenn.edu/software/ants/>; v2.2.0) and visually inspected for quality. Next, ANTS was used to spatially normalize individual data to the population template. Individual FA maps were again visually inspected to assure successful registration to the population FA template. Spatial transformations were subsequently applied to other DTI parameters, including mean, radial, and axial diffusivities (MD, RD, AD, respectively), as well as the map of diffusion tensors. Tensors were reoriented to adjust for this spatial transformation. A population-averaged tensor template was generated using the reoriented tensor maps and the TVMean tool as part of the DTI-TK software package (v2.3.3). Next, a white-matter mask was generated from the population-averaged FA template by thresholding at a value of 0.2 using fslmaths. Whole-brain tractography was performed using Camino’s deterministic tractography tool and the white matter mask as a seed. These tracts were then converted to a .trk file to allow viewing and further analyses in TrackVis (<http://www.trackvis.org/>; v0.6.1). From the whole-brain tractogram, the left and right uncinate fasciculi (UF) were manually delineated in TrackVis. Additional tracts and regions of interest from the IIT (Zhang & Arfanakis, 2018) and JHU (Mori et al., 2008) atlases were identified and warped into alignment of the population FA template by coregistering each atlas to the population template. IIT and JHU atlases were then resampled into the population template space through the application of these transforms, using nearest neighbor interpolation. Next, all tracts of interest (i.e. IIT, JHU, manually defined UF) were warped into each participant’s native space, using the inverse of the population spatial normalization transformations. Lastly, using AFNI “3dROIstat” (<https://afni.nimh.nih.gov/>) and native space images, average measures for FA, MD, RD, and AD were extracted for each tract in each subject, as well as for all voxels within the white-matter mask, providing both tract-specific and global values for the measures. For publication of the DTI processing, see Pedersen et al., 2021.

Below is a brief summary of the different measures from these models.

DTI measures (Alexander et al., 2011) - The following metrics are widely used:

- Fractional anisotropy (FA) - **[RA5WF...]** is the normalized standard deviation of the eigenvalues of the DTI. It is very sensitive to changes in white matter microstructure, but not very specific, as it can be influenced by changes in neurite density and dispersion among other factors. Lower FA is associated with aging.
- Mean diffusivity (MD) - **[RA5WM...]** is the average diffusivity across the three principal directions. It is affected by both membrane density and fluid viscosity. Higher values of MD are associated with aging.
- Radial diffusivity (RD) - **[RA5WR...]** measures diffusivity perpendicular to the axons. Higher values are associated with demyelination.
- Axial diffusivity (AD) - **[RA5WA...]** measures diffusivity along the axons. AD is influenced by several factors, including axonal density, axonal diameter, and

myelination, as well as the degree of water restriction along the fiber tract. Higher values of AD are associated with aging.

For the 118 participants with DWI data, the following metrics were calculated

- Global (white matter) values for the four DTI-based metrics **[RA5W_G...]**
- Tract-specific measures extracted using DTI-based white-matter atlases
 - JHU ICBM-DTI-81 v1.0 **[RA5W_J...]** (<http://cmrm.med.jhmi.edu/>; Hua et al., 2008; Mori et al., 2008; Wakana et al., 2007) with FSL v5.0.11 (<https://fsl.fmrib.ox.ac.uk/fsl/fslwiki/Atlases>)
 - IIT v4.1 **[RA5W_I...]** (<http://www.iit.edu/~mri/IITHumanBrainAtlas.html>; Zhang & Arfanakis 2018)
- Measures derived from population-based manual tractography of the uncinate fasciculus and fornix stria terminalis **[RA5W_T...]** are also provided.

VARIABLE NAMING

Partial variable names listed below. For more detailed information on variable names see atlas tables below or *MR1_P5_VARIABLE_NAMES_20260206*.

Scan type:

[RA5E...]: T1-weighted (Extracted structural measures)

[RA5W...]: Diffusion-weighted (Extracted diffusion weighted imaging measures)

Measurement type:

[RA5ET...]: Cortical Thickness (mm)

[RA5EC...]: Cortical Curvature (mm)

[RA5EA...]: Cortical Surface Area (mm²)

[RA5EV...]: Cortical Volume (mm³)

[RA5ES...]: Subcortical Volume (mm³)

[RA5WF...]: Fractional Anisotropy (FA)

[RA5WM...]: Mean Diffusivity (MD)

[RA5WR...]: Radial Diffusivity (RD)

[RA5WA...]: Axial Diffusivity (AD)

Hemisphere: Note that ‘_’ represents any one of the measurement variables listed above.

[RA5_ _G...]: Measurement is global (encompasses entire brain)

[RA5_ _L...]: Measurement is specific to left hemisphere

[RA5_ _R...]: Measurement is specific to right hemisphere

[RA5_ _N...]: Not applicable; measurement is bilateral

Atlas: Note that ‘_’ represents any one of the measurement and hemisphere variables listed above.

[RA5E_ _D...]: Measurement calculated using Destrieux brain atlas (Fischl et al., 2004b).

[RA5E_ _K...]: Measurement calculated using Desikan-Killiany brain atlas (Desikan et al., 2006).

[RA5E_ _T...]: Measurement calculated using Desikan-Killiany-Tourville brain atlas (Klein & Tourville, 2012).

[RA5E_ _A...]: Measurement calculated using FreeSurfer aseg subcortical brain atlas (Fischl et al., 2002) or Hippocampal Subfield (Iglesias et al., 2015) and Amygdala Nuclei (Saygin & Kliemann et al., 2017) module.

[RA5W_ _I...]: Measurement calculated using IIT v4.1 white matter atlas (Zhang & Arfanakis, 2018).

[RA5W__J...]: Measurement calculated using JHU white matter atlas (Hua et al., 2008; Mori et al., 2008; and Wakana et al., 2007).

[RA5W__T...]: Measurement calculated using manual tractography

Brain-Based Aging Algorithm:

[RA5EB]: Brain-Predicted Age (yrs) estimated using Cole brainageR v1.0 -

<https://github.com/james-cole/brainageR/tree/1.0>

[RA5EBC]: Brain-Predicted Age (yrs) estimated using Cole brainageR v2.0 -

<https://github.com/james-cole/brainageR/tree/2.0>

[RA5EBT]: Brain-Predicted Age (yrs) estimated using two-stage-age-network (TSAN) model from PMID: 34086565 - <https://github.com/Milan-BUAA/TSAN-brain-age-estimation>

[RA5EBP]: Brain-Predicted Age (yrs) estimated using 3D-CNN model from PMID: 36595679 -

https://github.com/irimia-laboratory/USC_BA_estimator

[RA5EBD]: DunedinPACNI Dunedin Pace of Aging Calculated from NeuroImaging from PMID: 40595015 - <https://github.com/etw11/DunedinPACNI>

ATLAS/MODULE TABLES

DESTRIEUX CORTICAL ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
G_and_S_frontomargin	Fronto-marginal gyrus (of Wernicke) and sulcus	RA5E__D01
G_and_S_occipital_inf	Inferior occipital gyrus (O3) and sulcus	RA5E__D02
G_and_S_paracentral	Paracentral lobule and sulcus	RA5E__D03
G_and_S_subcentral	Subcentral gyrus (central operculum) and sulci	RA5E__D04
G_and_S_transv_frontopol	Transverse frontopolar gyri and sulci	RA5E__D05
G_and_S_cingul-Ant	Anterior part of the cingulate gyrus and sulcus (ACC)	RA5E__D06
G_and_S_cingul-Mid-Ant	Middle-anterior part of the cingulate gyrus and sulcus (aMCC)	RA5E__D07
G_and_S_cingul-Mid-Post	Middle-posterior part of the cingulate gyrus and sulcus (pMCC)	RA5E__D08
G_cingul-Post-dorsal	Posterior-dorsal part of the cingulate gyrus (dPCC)	RA5E__D09
G_cingul-Post-ventral	Posterior-ventral part of the cingulate gyrus (vPCC, isthmus of the cingulate gyrus)	RA5E__D10
G_cuneus	Cuneus (O6)	RA5E__D11
G_front_inf-Opercular	Opercular part of the inferior frontal gyrus	RA5E__D12
G_front_inf-Orbital	Orbital part of the inferior frontal gyrus	RA5E__D13
G_front_inf-Triangul	Triangular part of the inferior frontal gyrus	RA5E__D14
G_front_middle	Middle frontal gyrus (F2)	RA5E__D15
G_front_sup	Superior frontal gyrus (F1)	RA5E__D16
G_ins_lg_and_S_cent_ins	Long insular gyrus and central sulcus of the insula	RA5E__D17
G_insular_short	Short insular gyri	RA5E__D18
G_occipital_middle	Middle occipital gyrus (O2, lateral occipital gyrus)	RA5E__D19
G_occipital_sup	Superior occipital gyrus (O1)	RA5E__D20
G_oc-temp_lat-fusifor	Lateral occipito-temporal gyrus (fusiform gyrus, O4-T4)	RA5E__D21
G_oc-temp_med-Lingual	Lingual gyrus, lingual part of the medial occipito-temporal gyrus, (O5)	RA5E__D22
G_oc-temp_med-Parahip	Parahippocampal gyrus, parahippocampal part of the medial occipito-temporal gyrus, (T5)	RA5E__D23
G_orbital	Orbital gyri	RA5E__D24
G_pariet_inf-Angular	Angular gyrus	RA5E__D25
G_pariet_inf-Supramar	Supramarginal gyrus	RA5E__D26
G_parietal_sup	Superior parietal lobule (lateral part of P1)	RA5E__D27
G_postcentral	Postcentral gyrus	RA5E__D28
G_precentral	Precentral gyrus	RA5E__D29
G_precuneus	Precuneus (medial part of P1)	RA5E__D30
G_rectus	Straight gyrus, Gyrus rectus	RA5E__D31
G_subcallosal	Subcallosal area, subcallosal gyrus	RA5E__D32
G_temp_sup-G_T_transv	Anterior transverse temporal gyrus (of Heschl)	RA5E__D33
G_temp_sup-Lateral	Lateral aspect of the superior temporal gyrus	RA5E__D34
G_temp_sup-Plan_polar	Planum polare of the superior temporal gyrus	RA5E__D35

G_temp_sup-Plan_tempo	Planum temporale or temporal plane of the superior temporal gyrus	RA5E__D36
G_temporal_inf	Inferior temporal gyrus (T3)	RA5E__D37
G_temporal_middle	Middle temporal gyrus (T2)	RA5E__D38
Lat_Fis-ant-Horizon	Horizontal ramus of the anterior segment of the lateral sulcus (or fissure)	RA5E__D39
Lat_Fis-ant-Vertical	Vertical ramus of the anterior segment of the lateral sulcus (or fissure)	RA5E__D40
Lat_Fis-post	Posterior ramus (or segment) of the lateral sulcus (or fissure)	RA5E__D41
Pole_occipital	Occipital pole	RA5E__D42
Pole_temporal	Temporal pole	RA5E__D43
S_calcarine	Calcarine sulcus	RA5E__D44
S_central	Central sulcus (Rolando's fissure)	RA5E__D45
S_cingul-Marginalis	Marginal branch (or part) of the cingulate sulcus	RA5E__D46
S_circular_insula_ant	Anterior segment of the circular sulcus of the insula	RA5E__D47
S_circular_insula_inf	Inferior segment of the circular sulcus of the insula	RA5E__D48
S_circular_insula_sup	Superior segment of the circular sulcus of the insula	RA5E__D49
S_collat_transv_ant	Anterior transverse collateral sulcus	RA5E__D50
S_collat_transv_post	Posterior transverse collateral sulcus	RA5E__D51
S_front_inf	Inferior frontal sulcus	RA5E__D52
S_front_middle	Middle frontal sulcus	RA5E__D53
S_front_sup	Superior frontal sulcus	RA5E__D54
S_interm_prim-Jensen	Sulcus intermedius primus (of Jensen)	RA5E__D55
S_intrapariet_and_P_trans	Intraparietal sulcus (interparietal sulcus) and transverse parietal sulci	RA5E__D56
S_oc_middle_and_Lunatus	Middle occipital sulcus and lunatus sulcus	RA5E__D57
S_oc_sup_and_transversal	Superior occipital sulcus and transverse occipital sulcus	RA5E__D58
S_occipital_ant	Anterior occipital sulcus and preoccipital notch (temporo-occipital incisure)	RA5E__D59
S_oc-temp_lat	Lateral occipito-temporal sulcus	RA5E__D60
S_oc-temp_med_and_Lingual	Medial occipito-temporal sulcus (collateral sulcus) and lingual sulcus	RA5E__D61
S_orbital_lateral	Lateral orbital sulcus	RA5E__D62
S_orbital_med-olfact	Medial orbital sulcus (olfactory sulcus)	RA5E__D63
S_orbital-H_Shaped	Orbital sulci (H-shaped sulci)	RA5E__D64
S_parieto_occipital	Parieto-occipital sulcus (or fissure)	RA5E__D65
S_pericallosal	Pericallosal sulcus (S of corpus callosum)	RA5E__D66
S_postcentral	Postcentral sulcus	RA5E__D67
S_precentral-inf-part	Inferior part of the precentral sulcus	RA5E__D68
S_precentral-sup-part	Superior part of the precentral sulcus	RA5E__D69
S_suborbital	Suborbital sulcus (sulcus rostrales, supraorbital sulcus)	RA5E__D70
S_subparietal	Subparietal sulcus	RA5E__D71
S_temporal_inf	Inferior temporal sulcus	RA5E__D72
S_temporal_sup	Superior temporal sulcus (parallel sulcus)	RA5E__D73
S_temporal_transverse	Transverse temporal sulcus	RA5E__D74

DESIKAN-KILLIANY CORTICAL ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
bankssts	Banks superior temporal sulcus	RA5E__K01
caudalanteriorcingulate	Caudal anterior-cingulate cortex	RA5E__K02
caudalmiddlefrontal	Caudal middle frontal gyrus	RA5E__K03
cuneus	Cuneus cortex	RA5E__K04
entorhinal	Entorhinal cortex	RA5E__K05
fusiform	Fusiform gyrus	RA5E__K06
inferiorparietal	Inferior parietal cortex	RA5E__K07
inferiortemporal	Inferior temporal gyrus	RA5E__K08
isthmuscingulate	Isthmus– cingulate cortex	RA5E__K09
lateraloccipital	Lateral occipital cortex	RA5E__K10
lateralorbitofrontal	Lateral orbital frontal cortex	RA5E__K11
lingual	Lingual gyrus	RA5E__K12
medialorbitofrontal	Medial orbital frontal cortex	RA5E__K13
middletemporal	Middle temporal gyrus	RA5E__K14
parahippocampal	Parahippocampal gyrus	RA5E__K15
paracentral	Paracentral lobule	RA5E__K16
parsopercularis	Pars opercularis	RA5E__K17
parsorbitalis	Pars orbitalis	RA5E__K18
parstriangularis	Pars triangularis	RA5E__K19
pericalcarine	Pericalcarine cortex	RA5E__K20
postcentral	Postcentral gyrus	RA5E__K21
posteriorcingulate	Posterior-cingulate cortex	RA5E__K22
precentral	Precentral gyrus	RA5E__K23
precuneus	Precuneus cortex	RA5E__K24
rostralanteriorcingulate	Rostral anterior cingulate cortex	RA5E__K25
rostralmiddlefrontal	Rostral middle frontal gyrus	RA5E__K26
superiorfrontal	Superior frontal gyrus	RA5E__K27
superiorparietal	Superior parietal cortex	RA5E__K28
superiortemporal	Superior temporal gyrus	RA5E__K29
supramarginal	Supramarginal gyrus	RA5E__K30
frontalpole	Frontal pole	RA5E__K31
temporalpole	Temporal pole	RA5E__K32
transversetemporal	Transverse temporal cortex	RA5E__K33
insula	Insula	RA5E__K34

DESIKAN-KILLIANY-TOURVILLE – DKT - CORTICAL ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
caudalanteriorcingulate	Caudal anterior-cingulate cortex	RA5E__T01
caudalmiddlefrontal	Caudal middle frontal gyrus	RA5E__T02
cuneus	Cuneus cortex	RA5E__T03

entorhinal	Entorhinal cortex	RA5E__T04
fusiform	Fusiform gyrus	RA5E__T05
inferiorparietal	Inferior parietal cortex	RA5E__T06
inferiortemporal	Inferior temporal gyrus	RA5E__T07
isthmuscingulate	Isthmus– cingulate cortex	RA5E__T08
lateraloccipital	Lateral occipital cortex	RA5E__T09
lateralorbitofrontal	Lateral orbital frontal cortex	RA5E__T10
lingual	Lingual gyrus	RA5E__T11
medialorbitofrontal	Medial orbital frontal cortex	RA5E__T12
middletemporal	Middle temporal gyrus	RA5E__T13
parahippocampal	Parahippocampal gyrus	RA5E__T14
paracentral	Paracentral lobule	RA5E__T15
parsopercularis	Pars opercularis	RA5E__T16
parsorbitalis	Pars orbitalis	RA5E__T17
parstriangularis	Pars triangularis	RA5E__T18
pericalcarine	Pericalcarine cortex	RA5E__T19
postcentral	Postcentral gyrus	RA5E__T20
posteriorcingulate	Posterior-cingulate cortex	RA5E__T21
precentral	Precentral gyrus	RA5E__T22
precuneus	Precuneus cortex	RA5E__T23
rostralanteriorcingulate	Rostral anterior cingulate cortex	RA5E__T24
rostralmiddlefrontal	Rostral middle frontal gyrus	RA5E__T25
superiorfrontal	Superior frontal gyrus	RA5E__T26
superiorparietal	Superior parietal cortex	RA5E__T27
superiortemporal	Superior temporal gyrus	RA5E__T28
supramarginal	Supramarginal gyrus	RA5E__T29
transversetemporal	Transverse temporal cortex	RA5E__T30
insula	Insula	RA5E__T31

ASEG SUBCORTICAL ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
Lateral-Ventricle	Lateral Ventricle	RA5ES_A09
Inf-Lat-Vent	Inferior Lateral Ventricle	RA5ES_A08
Cerebellum-White-Matter	Cerebellum White Matter	RA5ES_A05
Cerebellum-Cortex	Cerebellum Cortex	RA5ES_A04
Thalamus-Proper	Thalamus	RA5ES_A12
Caudate	Caudate	RA5ES_A03
Putamen	Putamen	RA5ES_A11
Pallidum	Pallidum	RA5ES_A10
Hippocampus	Hippocampus	RA5ES_A07
Amygdala	Amygdala	RA5ES_A02
Accumbens-area	Accumbens Area	RA5ES_A01
VentralDC	Ventral Diencephalon	RA5ES_A13

vessel	vessel (non-specific)	RA5ES_A14
3rd-Ventricle	Third Ventricle	RA5ESNA01
4th-Ventricle	Fourth Ventricle	RA5ESNA02
Brain-Stem	Brain Stem	RA5ESNA03
CSF	Cerebrospinal Fluid	RA5ESNA15
choroid-plexus	Choroid Plexus	RA5ES_A06
CortexVol	Cortical Gray Matter Volume	RA5ES_A15 OR RA5ESNA13
CorticalWhiteMatterVol*	Cortical White Matter Volume*	RA5ES_A16 OR RA5ESNA14
SurfaceHoles	Number of defect holes in surfaces prior to fixing	RA5ES_A17 OR RA5ESNA24
BrainSegVol	Brain Segmentation Volume	RA5ESNA04
BrainSegVol-to-eTIV	Ratio of BrainSegVol to estimated Total Intracranial Volume	RA5ESNA05
BrainSegVolNotVent	Brain Segmentation Volume Without Ventricles	RA5ESNA06
BrainSegVolNotVentSurf	Brain Segmentation Volume Without Ventricles from Surf	RA5ESNA07
CC_Anterior	Anterior Corpus Callosum	RA5ESNA08
CC_Central	Central Corpus Callosum	RA5ESNA09
CC_Mid_Anterior	Mid-Anterior Corpus Callosum	RA5ESNA10
CC_Mid_Posterior	Mid-Posterior Corpus Callosum	RA5ESNA11
CC_Posterior	Posterior Corpus Callosum	RA5ESNA12
EstimatedTotalIntraCranialVol	Estimated Total Intracranial Volume	RA5ESNA16
MaskVol	Mask Volume	RA5ESNA17
MaskVol-to-eTIV	Ratio of MaskVol to estimated Total Intracranial Volume	RA5ESNA18
Optic-Chiasm	Optic Chiasm	RA5ESNA19
SubCortGrayVol	Subcortical Gray Matter Volume	RA5ESNA20
SupraTentorialVol	Supratentorial Volume	RA5ESNA21
SupraTentorialVolNotVent	Supratentorial Volume Without Ventricles	RA5ESNA22
SupraTentorialVolNotVentVox	Supratentorial Volume Voxel Count	RA5ESNA23
TotalGrayVol	Total Gray Matter Volume	RA5ESNA25

*FreeSurfer creators renamed variable from “CorticalWhiteMatterVol” in FreeSurfer v5.3.0 (used for MR1) to “CerebralWhiteMatterVol” in FreeSurfer v6.0.0 (used for M3). Same variable meaning, only change in naming convention.

AMYGDALA ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
Lateral-nucleus	Lateral nucleus	RA5ES_A18
Basal-nucleus	Basal nucleus	RA5ES_A19
Accessory-basal-nucleus	Accessory basal nucleus	RA5ES_A20
Anterior-amygdaloid-area-AAA	Anterior amygdaloid area	RA5ES_A21
Central-nucleus	Central nucleus	RA5ES_A22
Medial-nucleus	Medial nucleus	RA5ES_A23

Cortical-nucleus	Cortical nucleus	RA5ES_A24
Corticoamygdaloid-transitio	Corticoamygdaloid transition area	RA5ES_A25
Paralaminar-nucleus	Paralaminar nucleus	RA5ES_A26
Whole_amygdala	Amygdala	RA5ES_A27

HIPPOCAMPUS ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
Hippocampal_tail	Hippocampal tail	RA5ES_A28
Subiculum-body	Subiculum (body)	RA5ES_A29
CA1-body	Cornu ammonis 1 (body)	RA5ES_A30
Subiculum-head	Subiculum (head)	RA5ES_A31
Hippocampal-fissure	Hippocampal fissure	RA5ES_A32
Presubiculum-head	Presubiculum (head)	RA5ES_A33
CA1-head	Cornu ammonis 1 (head)	RA5ES_A34
Presubiculum-body	Presubiculum (body)	RA5ES_A35
Parasubiculum	Parasubiculum	RA5ES_A36
Molecular_layer_HP-head	Molecular layer (head)	RA5ES_A37
Molecular_layer_HP-body	Molecular layer (body)	RA5ES_A38
GC-ML-DG-head	Granule cell (GC) and molecular layer (ML) of the dentate gyrus (DG) (head)	RA5ES_A39
CA3-body	Cornu ammonis 3 (body)	RA5ES_A40
GC-ML-DG-body	Granule cell (GC) and molecular layer (ML) of the dentate gyrus (DG) (body)	RA5ES_A41
CA4-head	Cornu ammonis 4 (head)	RA5ES_A42
CA4-body	Cornu ammonis 4 (body)	RA5ES_A43
Fimbria	Fimbria	RA5ES_A44
CA3-head	Cornu ammonis 3 (head)	RA5ES_A45
HATA	Hippocampus-amygdala-transition-area	RA5ES_A46
Whole_hippocampal_body	Hippocampal body	RA5ES_A47
Whole_hippocampal_head	Hippocampal head	RA5ES_A48
Whole_hippocampus	Hippocampus	RA5ES_A49

JHU WHITE MATTER BUNDLES ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
Anterior_corona_radiata	Anterior corona radiata	RA5W__J01
Anterior_limb_of_internal_capsule	Anterior limb of internal capsule	RA5W__J02
Cerebral_peduncle	Cerebral peduncle	RA5W__J03
Cingulum_(cingulate_gyrus)	Cingulum (cingulate gyrus)	RA5W__J04
Cingulum_(hippocampus)	Cingulum (hippocampus)	RA5W__J05
Corticospinal_tract	Corticospinal tract	RA5W__J06

External_capsule	External capsule	RA5W_ _J07
Fornix_(cres)_-_Stria_terminalis_ (can_not_be_resolved_with_current_resolution)	Fornix (cres) / Stria terminalis (cannot be resolved with current resolution)	RA5W_ _J08
Inferior_cerebellar_peduncle	Inferior cerebellar peduncle	RA5W_ _J09
Medial_lemniscus	Medial lemniscus	RA5W_ _J10
Posterior_corona_radiata	Posterior corona radiata	RA5W_ _J11
Posterior_limb_of_internal_capsule	Posterior limb of internal capsule	RA5W_ _J12
Posterior_thalamic_radiation_ (include_optic_radiation)	Posterior thalamic radiation (includes optic radiation)	RA5W_ _J13
Retrolenticular_part_of_internal_capsule	Retrolenticular part of internal capsule	RA5W_ _J14
Sagittal_stratum_(include_inferior_longitudinal_fasciculus_and_inferior_fronto-occipital_fasciculus)	Sagittal stratum (includes inferior longitudinal fasciculus and inferior fronto-occipital fasciculus)	RA5W_ _J15
Superior_cerebellar_peduncle	Superior cerebellar peduncle	RA5W_ _J16
Superior_corona_radiata	Superior corona radiata	RA5W_ _J17
Superior_fronto-occipital_fasciculus_ (could_be_a_part_of_anterior_internal_capsule)	Superior fronto-occipital fasciculus (could be a part of anterior internal capsule)	RA5W_ _J18
Superior_longitudinal_fasciculus	Superior longitudinal fasciculus	RA5W_ _J19
Tapetum	Tapetum	RA5W_ _J20
Uncinate_fasciculus	Uncinate fasciculus	RA5W_ _J21
Body_of_corpus_callosum	Body of corpus callosum	RA5W_NJ01
Fornix_(column_and_body_of_fornix)	Fornix (column and body of fornix)	RA5W_NJ02
Genu_of_corpus_callosum	Genu of corpus callosum	RA5W_NJ03
Middle_cerebellar_peduncle	Middle cerebellar peduncle	RA5W_NJ04
Pontine_crossing_tract_(a_part_of_MCP)	Pontine crossing tract (a part of MCP)	RA5W_NJ05
Splenium_of_corpus_callosum	Splenium of corpus callosum	RA5W_NJ06

IIT V4.1 WHITE MATTER BUNDLES ATLAS

VARIABLE LABEL (FROM SPSS FILE)	FULL NAME OF PARCELLATION	VARIABLE NAME
Lcing	Left cingulum (cingulate gyrus portion)	RA5W_L01
Lcing2	Left cingulum (hippocampal portion)	RA5W_L02
Lcst	Left corticospinal tract	RA5W_L03
Lifo	Left inferior fronto-occipital fasciculus	RA5W_L04
Lilf	Left inferior longitudinal fasciculus	RA5W_L05
Lslf	Left superior longitudinal fasciculus	RA5W_L06
Lunc	Left uncinate fasciculus	RA5W_L07
Rcing	Right cingulum (cingulate gyrus portion)	RA5W_R01
Rcing2	Right cingulum (hippocampal portion)	RA5W_R02
Rcst	Right corticospinal tract	RA5W_R03
Rifo	Right inferior fronto-occipital fasciculus	RA5W_R04
Rilf	Right inferior longitudinal fasciculus	RA5W_R05
Rslf	Right superior longitudinal fasciculus	RA5W_R06
Runc	Right uncinate fasciculus	RA5W_R07

Fmajor	Forceps major	RA5W_N01
Fminor	Forceps minor	RA5W_N02
Fornix	Fornix	RA5W_N03

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