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Collegiate athlete brain data for white matter mapping and network neuroscience

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Abstract **(126/170 words, no references)**

We describe a dataset of processed data with associated reproducible preprocessing pipeline collected from two collegiate athlete groups and one non-athlete group. The dataset shares minimally processed diffusion-weighted magnetic resonance imaging (dMRI) data, three models of the diffusion signal in the voxel, full-brain tractograms, segmentation of the major white matter tracts as well as structural connectivity matrices. There is currently a paucity of similar datasets openly shared. Furthermore, major challenges are associated with collecting this type of data. The data and derivatives shared here can be used as a reference to study the effects of long-term exposure to collegiate athletics, such as the effects of repetitive head impacts. We use advanced anatomical and dMRI data processing methods publicly available as reproducible web services at brainlife.io.

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Background & Summary (466/700 words)

Elite athletes are highly motivated individuals with physical and psychological characteristics that make them uniquely fit to compete in a sport. Understanding the impact of sports (positive as well as negative) to the brain is an ongoing and active research need (Bahrami et al., 2016; Brunetta et al., 2020; Chaddock-Heyman et al., 2018; Churchill, Caverzasi, et al., 2017; Churchill, Hutchison, et al., 2017; Davenport et al., 2016; Deng et al., 2018; El-Sayes et al., 2019; Esteban-Cornejo et al., 2019; Hänggi et al., 2010, 2015; Hillman et al., 2008; Hötting & Röder, 2013; Jäncke et al., 2009; Lefebvre et al., 2020; Mayer et al., 2017; Mayinger et al., 2018; Montenigro et al., 2017; Penedo & Dahn, 2005; Radak et al., 2013; Reimers et al., 2012; Ruotsalainen et al., 2020; Saraulli et al., 2017; Seo et al., 2019; Slobounov et al., 2017; Voss et al., 2011). Advancing understanding of the effects of sports on the brain is currently hindered by a lack of openly shared datasets and the challenge of collecting data from elite athletes. Our datasets address this challenge by providing magnetic resonance imaging data from 33 athletes and 9 matched controls. As of today, this is the first publicly available and openly shared datasets of college-level athletes.

Relatively recently, efforts to generate large-scale neuroimaging datasets to study the effects of sport on the brain have been funded. Take for example, trackTBI (Yue et al., 2013), ENIGMA (Koerte et al., 2020), and the CARE consortium (Broglio et al., 2017), which are large scale projects involving multiple investigators and institutions. To contribute to the advancement of science, a good percentage of the data in these projects is or is planned-to-be released for sharing. Because of the administrative burden and funding models, these datasets share data with several restrictions spanning all the way from requirements for co-authorship, study participation or research partnership. Our dataset is different, as we collected a smaller sample of subjects (42) from a single institution and shared the data set openly without administrative overhead.

We share the data utilizing a recently developed unique approach that exploits the free and secure cloud computing platform brainlife.io. The approach integrates, into a single record, both data and reproducible web-services implementing the full processing pipeline (Avesani et al., 2019; Stewart et al., 2015; Towns et al., 2014). The raw data contains both anatomical (T1 weighted) and diffusion-weighted (dMRI) magnetic resonance imaging data. The processed data contains 14 types of derivatives across 42 participants, comprising of 84 brain masks (2 per participant), 42 Freesurfer outputs (1 per participant), 168 fiber orientation dispersion (FOD) images (4 per participant), 588 diffusion parameter maps (14 per participant), 42 tractograms (1 per participant), 2,562 segmented major tracts (61 per participant), 756 connectivity matrices (18 per participant), and 42 cortex map datatypes (1 per participant). The total size of the repository is approximately 676.08 GB of data derivatives comprising 1470 datasets.

The processing pipeline implemented to process this dataset utilizes mainstream neuroimaging software libraries including FSL (Mark Jenkinson et al., 2012; S. M. Smith et al., 2004; Woolrich et al., 2009), FreeSurfer (A. Dale et al., 1999; A. M. Dale & Sereno, 1993; Desikan et al., 2006; B. Fischl et al., 2001, 2002; Bruce Fischl, Salat, et al., 2004; Bruce Fischl, Sereno, & Dale, 1999; Bruce Fischl, Sereno, Tootell, et al., 1999; Bruce Fischl, van der Kouwe, et al., 2004; Bruce Fischl & Dale, 2000; Han et al., 2006; Jovicich et al., 2006; Kuperberg et al., 2003; Reuter et al., 2010, 2012; Reuter & Fischl, 2011; Rosas et al., 2002; Salat et al., 2004; Segonne et al., 2004, 2007), MRTrix 3.0 (Tournier et al., 2019), DIPY (Garyfallidis et al., 2014), and connectome_workbench (Van Essen et al., 2013). The corresponding brainlife.io Apps were developed with a light-weight specification and utilizing modern methods for software containerization making the analyses trackable, reproducible, and reusable on a wide range of computing resources (Merkel, 2014). The present descriptor describes the repository and pipelines published via *brainlife.io* mechanisms. These resources will allow the broader research community to explore the effects of long-term sports participation by exploring high-quality preprocessed neuroimaging, replicate previous examinations of the data, and examine a wide variety of hypotheses without the impediment of the aforementioned barriers.

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Methods

Data sources

Data was upcycled (Vearncombe et al., 2017) from Caron *et al.* (*in review*) and is publicly available at https://doi.org/10.25663/brainlife.pub.14.

Neuroimaging data sources. Data were collected at the Indiana University Imaging Research Facility (IRF, https://www.indiana.edu/~irf). Data collection was approved by the Indiana University Institutional Review Board.

Study participants. A total of fifty-one male participants participated in the study. Twenty-one participants were 4th and 5th-year varsity Indiana University (IU) football "starters" (age 21.1 ± 1.5 years). This number accounts for approximately 60% of the total IU football team active players matching our criteria. Potential participants were excluded if they reported a diagnosed concussion within 6 months of the beginning of the study. One football player did not complete the study, and three football players did not complete the diffusion MRI (dMRI) scans. This left 17 usable datasets from the Football group. Following scanning, football players received a socioeconomic status survey gathering information regarding estimated family income and the area in which they were raised (i.e. urban, small town, suburbs). Nineteen members of the IU cross-country running team (age 20.2 ± 2.5 years) were included as a non-collision sports group and were matched to the football players based on age and experience level. Three of the players' anatomical (T1w) images were unusable and thus their data was not included. This left us with 16 eligible members. Our access to the socioeconomic status of non-athlete undergraduates was limited to Psychology and Neuroscience undergraduates who had filled out the socioeconomic survey in an IRB approved subject pool. Eleven controls (non-athletes) participants were selected from the limited pool matched to the football players (age 19.9 ± 3). Two of the controls' diffusion data contained artifacts that were beyond correction with our processing protocol and thus their data were not included, leaving nine usable datasets. Overall, the released dataset contains usable data from 17 football players, 16 cross-country runners, and 9 non-athletes for analysis (N = 42). In regards to concussion history, two football players had been diagnosed with a concussion approximately 3 years before the study and one player had been diagnosed approximately 2 years before the study. There was no history of concussion in the cross-country runners while at IU. No information was collected regarding the concussion history of the participants before their arrival at IU, however. Although we did not have this information available, we can estimate around 7.25% of football players have been diagnosed with a concussion prior to college given estimates from the literature (Dompier et al., 2015). Participants gave informed written consent that was approved by the Indiana University Institutional Review Board. All participants were recruited through flyers handed out by the athletic trainers of each team or posted around campus. Participants were compensated for participation with a cash payment.

Neuroimaging parameters. Participants were imaged using a 3-Tesla TIM Trio scanner located in the Imaging Research Facility at Indiana University. A 12-channel head coil was used as the 32-channel coil did not fit the heads of our larger subjects. Diffusion-weighted magnetic resonance imaging (dMRI) data were collected with two phase-encoding schemes, i.e anterior-posterior (AP) and posterior-anterior (PA). The following parameters were used for the dMRI pulse sequence: TR/TE = 4930/99.6 ms, iPAT acceleration factor = 2; voxel size = 2x2x2 mm isotropic, 143 diffusion-weighting directions, including sixty-four directions with b = 1000 s/mm^2 and sixty-four directions with b = 2000 s/mm^2. Fifteen non-weighted images were also acquired (b = 0). On T1-weighted (T1w) anatomical image was acquired for each participant using the following sequence: TR/TE = 1800/2.67 ms, TI = 900 ms, flip angle = 9°, bandwidth = 150 Hz/pixel, 160 sagittal slices, FOV = 256 mm, matrix = 256x256, slice thickness = 1 mm, resulting in 1 mm isotropic voxels.

Anatomical (T1w) preprocessing. Raw anatomical (T1w) images were preprocessed using the *fsl_anat* functionality provided by the FMRIB Software Library (FSL) (Mark Jenkinson et al., 2012; S. M. Smith et al., 2004; Woolrich et al., 2009) implemented as brainlife.io app brainlife.app.273. In brief, the raw anatomical (T1w) images were cropped and reoriented to match the orientation of the MNI152 template. Then, the cropped and reoriented images were *linearly* and *non-linearly* aligned to the MNI152 0.8mm template using *flirt* and *fnirt* respectively (Greve & Fischl, 2009; Mark Jenkinson et al., 2002; M. Jenkinson & Smith, 2001). The *linearly* aligned images will hereafter

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be referred to as the 'acpc aligned' anatomical (T1w) images. The warps generated from the *non-linear* alignment were subsequently used for mapping diffusion metrics to the cortex(Fukutomi et al., 2018). Following alignment, the 'acpc aligned' anatomical (T1w) images were processed via Freesurfer's *recon-all* function to generate pial (i.e. cortical) and white matter surfaces and to parcellate the brain into known anatomical atlases (A. Dale et al., 1999; A. M. Dale & Sereno, 1993; Desikan et al., 2006; B. Fischl et al., 2001, 2002; Bruce Fischl, Salat, et al., 2004; Bruce Fischl, Sereno, & Dale, 1999; Bruce Fischl, Sereno, Tootell, et al., 1999; Bruce Fischl, van der Kouwe, et al., 2004; Bruce Fischl & Dale, 2000; Han et al., 2006; Jovicich et al., 2006; Kuperberg et al., 2003; Reuter et al., 2010, 2012; Reuter & Fischl, 2011; Rosas et al., 2002; Salat et al., 2004; Segonne et al., 2004, 2007) implemented as brainlife.io app brainlife.app.0. The Destrieux (aparc.a2009s) atlas was used for subsequent white matter tract segmentation and for mapping of diffusion metrics to the cortical surface (Destrieux et al., 2010). For network generation, the multi-modal 180 cortical node parcellation (Glasser et al., 2016) was mapped to the Freesurfer segmentation of each participant implemented as brainlife.io app brainlife.app.23. Finally, the 'acpc aligned' anatomical (T1w) image was segmented into different tissue-types using MRTrix 3.0's *5ttgen* functionality (Segonne et al., 2007; Tournier et al., 2019) implemented as brainlife.io app brainlife.app.239. The gray- and white-matter interface mask was subsequently used as a seed mask for white matter tractography.

Diffusion (dMRI) preprocessing. Raw dMRI images were first reoriented to match the orientation of the MNI152 template using the fslreorient2std command provided by FSL. The opposite-facing distortions corresponding to each phase encoding direction (i.e. PA and AP) were then combined into a single corrected image in a method similar to the one described in Andersson and colleagues (2003) (Andersson et al., 2003; S. M. Smith et al., 2004) (i.e. top-up command) as provided by FSL (Mark Jenkinson et al., 2012; Woolrich et al., 2009). Eddy-current and motion correction was then applied via the *eddy_cuda8.0* with replacement of outlier slices (*i.e. repol*) command provided by FSL (Andersson et al., 2016, 2017, 2018; Andersson & Sotiropoulos, 2016). *Eddy_quad* was then used to generate quality assurance measures of the dMRI images, including measures of temporal signal-to-noise ratio (i.e. tSNR) and motion (Bastiani et al., 2019). The preceding steps were implemented as brainlife.io app brainlife.app.287. MRTrix 3.0's *dwigradcheck* functionality was used to check and correct for potential misaligned gradient vectors following top-up and eddy (Jeurissen, Leemans, et al., 2014). Following this, dMRI images were debiased using ANT's *n4* functionality (Tustison et al., 2014) and the background noise was cleaned using MRTrix 3.0's *dwidenoise* functionality (Veraart et al., 2016). Finally, the preprocessed dMRI images were registered to the 'acpc aligned' anatomical (T1w) image using FSL's *epi_reg* functionality (Greve & Fischl, 2009; Mark Jenkinson et al., 2002; M. Jenkinson & Smith, 2001) and resliced to 1mm isotropic voxels. The preceding steps were implemented as brainlife.io app brainlife.app.68. Brainmasks of the preprocessed, acpc-aligned dMRI images were then used for subsequent modelling and tractography using FSL's *bet2* functionality. Masks from three participants were manually-edited in order to remove excess non-brain material (S. M. Smith, 2002) implemented as brainlife.io App brainlife.app.163.

Quality control was estimated by calculating the Signal to Noise Ratio (SNR) of the diffusing data. To quantify the SNR in the preprocessed, acpc-aligned dMRI data, the workflow provided by Dipy to map SNR in the corpus callosum was used (Descoteaux et al., 2011; Garyfallidis et al., 2014; Jones et al., 2013) implemented as brainlife.io app brainlife.app.120. SNR values reported are generated from this step.

White matter microstructure modeling (DTI). In order to investigate advanced microstructural properties of white matter, the diffusion tensor (DTI) model was fit to the preprocessed, acpc-aligned dMRI data using FSL's *dtifit* functionality implemented as brainlife.io app brainlife.app.292. For white matter tract profiles, the default parameters of *dtifit* were used and the b = 1000 shell was chosen for fitting. However, for mapping of the DTI measures to the cortex, both the b = 1000 and b = 2000 shells were used, kurtosis was calculated, and the sum of squared errors was outputted following the parameters used in Fukutomi et al (Fukutomi et al., 2018).

White matter microstructure modeling (NODDI). In order to investigate advanced microstructural properties of white matter, the Neurite Orientation Dispersion and Density Imaging (NODDI) (Zhang et al., 2012) model was fit to the multi-shell (i.e. b = 1000, 2000 s/mm^2) acpc-aligned dMRI data via the Accelerated Microstructure Imaging via Convex Optimization (AMICO; https://github.com/daducci/AMICO; (Daducci et al., 2015)) toolbox implemented as brainlife.io app brainlife.app.365. The AMICO toolbox was used in order to significantly speed-up the time necessary to fit the NODDI model by reformulating the NODDI model as a linear system, without sacrificing

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accuracy (Daducci et al., 2015). For major white matter tract analysis, the isotropic diffusivity parameter (d_{iso}) was set to 3.0x10-3 m^2/s (the rate of unhindered diffusion of water) while the intrinsic free diffusivity parameter ($d_{//}$) was set to 1.7x10-3 mm^2/s. For cortical white matter parcel analyses, the isotropic diffusivity parameter was also set to 3.0x10-3 mm^2/s while the intrinsic free diffusivity parameter was set to 1.1x10-3 mm^2/s, which is the optimal value of diffusivity found by Fukutomi et al (Fukutomi et al., 2018).

White matter microstructure modeling (CSD). The CSD model was fit to the preprocessed multi-shell data utilizing MRTrix 3.0 dwi2fod function across 4 maximum spherical harmonic orders (i.e. L_{max}) parameters (2,4,6,8) implemented as brainlife.io app brainlife.app.238 (Jeurissen, Leemans, et al., 2014; Jeurissen, Tournier, et al., 2014; Takemura et al., 2016; Tournier et al., 2004). L_{max}'s 6 and 8 were chosen for subsequent white matter tractography, however, all L_{max}'s are included in the released data.

White matter microstructure modeling (Tractography). Anatomically-constrained probabilistic tractography (ACT) (R. E. Smith et al., 2012) via MRTrix3's *tckgen* functionality implemented as brainlife.io app brainlife.app.297 was used to generate tractograms on preprocessed multi-shell dMRI data for each participant. A total of 1.5 million was tracked over both lmax6 and lmax8. The two tractograms were then combined to create a single tractogram of 3 million streamlines via Vistasoft functionality implemented as brainlife.io app brainlife.app.305. The step-size was set to 0.2mm for both lmax6 and lmax8. The minimum length of streamlines was set to 25mm, and the maximum length was set to 250mm. A maximum angle of curvature of 35° was set. The merged tractogram of 3 million streamlines was then used for subsequent white matter tract segmentation and network generation.

White matter microstructure modeling (Segmentation & Cleaning). 61 human white matter tracts were segmented using a custom version of the white matter query language (Bullock et al., 2019) implemented as brainlife.io app brainlife.app.188. These tracts include the following: L/R arcuate, aslant, corticospinal tract (CST), contralateral anterior frontal cerebellar tracts, contralateral motor cerebellar tracts, inferior fronto-occipital fasciculus (IFOF), inferior longitudinal fasciculus (ILF), middle longitudinal fasciculus-angular gyrus (MDLF-ang) and-superior parietal lobule (MDLF-spl), motor cerebellar tracts, occipital cerebellar tracts, superior longitudinal fasciculus components 1&2 and 3 (SLF-1&2, SLF-3), temporal-parietal connection, thalamic cerebellar tracts, uncinate, vertical occipital fasciculus (VOF), Baum's and Meyers' loops, cingulum, frontal thalamic tracts, motor thalamic tracts, parietal arcuate (pArc), parietal thalamic tracts, spinothalamic tracts, and temporal thalamic tracts. The callosal tracts, including anterior frontal, forceps major, forceps minor, middle frontal, and parietal corpus callosum, are also included.

Following tract segmentation, outlier streamlines were removed using mba's *mbaComputeFibersOutliers* functionality (Pestilli et al., 2014) implemented as brainlife.io app brainlife.app.195. For each tract, the spatial 'core' representation of the tract was computed by averaging the streamline coordinates across all streamlines in a tract. Streamlines were removed if their length was 4 standard deviations from the length of the 'core' representation and/or were located 4 standard deviations away from the 'core' representation of the tract. The cleaned segmentations were then used for all subsequent analyses.

White matter microstructure modeling (Tract profiles): Tract profiles (Yeatman et al., 2012) for each DTI parameter estimate (i.e. AD, FA, MD, RD) and NODDI parameter estimate (i.e. NDI, ODI, ISOVF) were generated by estimating the "core" representation of each tract, resampling and segmenting each streamline into 200 equally-spaced nodes, applying a gaussian weight to each streamline based on the distance away from the "core", and obtaining the weighted average metric at each node. This was performed using MATLAB code utilizing the Compute_FA_AlongFG command provided by Vistasoft (https://github.com/vistalab/vistasoft) implemented as brainlife.io app brainlife.app.361.

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White matter network modeling (Network generation). Structural networks were generated using the multi-modal 180 cortical node atlas and the merged tractograms for each participant using MRTrix3's *tck2connectome (R. E. Smith et al., 2015a)* and *tcksift2 (R. E. Smith et al., 2015b)* functionality implemented as brainlife.io app brainlife.app.394. SIFT2 was used to generate a cross-sectional area weight value for each streamline in order to accurately reflect density. Connectomes were then generated by computing the number of streamlines intersecting each ROI pairing in the 180 cortical node parcellation. Multiple adjacency matrices were generated, including: count, density (i.e. count divided by the node volume of the ROI pairs), length, length density (i.e. length divided by the volume of the ROI pairs), and average and average density AD, FA, MD, RD, NDI, ODI, and ISOVF. Density matrices were generated using the *-invnodevol* option (Hagmann et al., 2008). For non-count measures (length, AD, FA, MD, RD, NDI, ODI, ISOVF), the average measure across all streamlines connecting and ROI pair was computed using MRTrix3's *tck2scale* functionality using the *-precise* option (R. E. Smith et al., 2013) and the *-scale_file* option in *tck2connectome*. These matrices can be thought of as the "average measure" adjacency matrices.

Cortical white matter microstructure modeling (Cortex mapping). DTI and NODDI measures were mapped to each participant's cortical white matter parcels following methods found in Fukutomi and colleagues (Fukutomi et al., 2018) using functions provided by Connectome Workbench (Van Essen et al., 2013) implemented as brainlife.io app brainlife.app.379. First, mid-thickness surfaces between the cortical pial surface and white matter surface provided by Freesurfer segmentation were computed using the wb_command -surface-cortex-layer function provided by Workbench command. A Gaussian smoothing kernel (FWHM = ~4mm, σ = 5/3mm) was applied along the axis normal to the surface, and DTI and NODDI measures were mapped using the wb_command -volume-to-surface-mapping function. Freesurfer was used to map the average NODDI parameter estimates to subcortical white matter parcels.

Data visualization.
A majority of the images generated for this descriptor were generated using a number of brainlife.io applications utilizing functionality from FSL and DIPY. A list of these Apps include: Generate images of NODDI/DTI, Generate figures of whole-brain tractogram (TCK), Generate images of mask overlaid on DWI, Generate an image of ODF, Generate images of DWI overlaid on T1, Generate images of tissue type masks, Generate images of T1/DWI, and Plot response function. The other images were generated using brainlife.io's visualization functionality.

Application	Github repository	Open Service DOI	Git branch
Brain Alignment	https://github.com/brainlife/app-fsl-anat	https://doi.org/10.25663/brainlife.app.273	v1.0
Cortical and Subcortical Segmentation	https://github.com/brain-life/app-freesurfer	https://doi.org/10.25663/bl.app.0	1.11
White matter Tissue Segmentation	https://github.com/brainlife/app-mrtrix3-5tt	https://doi.org/10.25663/brainlife.app.239	binarize-v1.0
Multi-Atlas Transfer Tool (MaTT)	https://github.com/faskowit/app-multiAtlasTT	https://doi.org/10.25663/bl.app.23	0.0.5
dMRI artifacts removal	https://github.com/brainlife/app-FSLTopupEddy	https://doi.org/10.25663/brainlife.app.287	cuda-v1.0
dMRI proporcessing and model fitting	https://github.com/brain-life/app-mrtrix3-preproc	https://doi.org/10.25663/bl.app.68	1.6
SNR Calculation	https://github.com/davhunt/app-snr_in_cc/tree/plot	https://doi.org/10.25663/bl.app.120	plot
Brain mask Generation	https://github.com/brain-life/app-FSLBET	https://doi.org/10.25663/brainlife.app.163	dwi
NODDI model fit	https://github.com/brain-life/app-noddi-amico	https://doi.org/10.25663/brainlife.app.365	1.3
Diffusion Tensor Fit	https://github.com/brainlife/app-fslDTIFIT	https://doi.org/10.25663/brainlife.app.292	v1.0
Constrained Spherical	https://github.com/bacaron/app-mrtrix3-act	https://doi.org/10.25663/brainlife.app.238	csd_generation-v 1.0

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Deconvolution Fit			
Tractography	https://github.com/bacaron/app-mrtrix3-act	https://doi.org/10.25663/brainlife.app.297	1.3
Merging Tractography Files	https://github.com/bacaron/app-mergeTCK	https://doi.org/10.25663/brainlife.app.305	two-tck
White Matter Anatomy Segmentation	https://github.com/brainlife/app-wmaSeg	https://doi.org/10.25663/brainlife.app.188	3.7
Remove Tract Outliers	https://github.com/brainlife/app-removeTractOutliers	https://doi.org/10.25663/brainlife.app.195	1.3
Tract Profiles	https://github.com/brain-life/app-tractanalysisprofiles	https://doi.org/10.25663/brainlife.app.361	1.8
Cortex Tissue Mappin	https://github.com/brainlife/app-cortex-tissue-mapping	https://doi.org/10.25663/brainlife.app.379	v1.1
Structural Connectome	https://github.com/brainlife/app-sift2-connectome-generation	https://doi.org/10.25663/brainlife.app.394	sift2_v1.0

Table 1. Description and web-links to the open-source code and open cloud services used in the creation of this dataset.

Data Records

The data outputs on brainlife.io are organized using https://brainlife.io/datatypes. These DataTypes allow applications to exchange and archive data. Data outputs can be conveniently downloaded from brainlife.io using the BIDS standard(Gorgolewski et al., 2016). The standard does not yet provide a specification for processed dMRI, tractograms, white matter tracts, and connectivity matrices. The brainlife.io platform will be updated as soon as the BIDS standard fully describes a specification for the models and tractography, tractometry, and network data. For the time being the specification follows the work previous work (Avesani et al., 2019):

T1-weighted Anatomical. T1w image preprocessed and linearly- and nonlinearly- aligned to the MNI152 0.8 MM template using FMRIB Software Library (FSL)'s *fsl_anat* functionality.

```
upload/sub-{}/anat/
      sub-{}_tag-preprocessed_tag-acpc-aligned_desc-{}_T1w.json
      sub-{}_tag-preprocessed_tag-acpc-aligned_desc-{}_T1w.nii.gz
      sub-{}_tag-preprocessed_tag-standard_desc-{}_T1w.json
      sub-{}_tag-preprocessed_tag-standard_desc-{}_T1w.nii.gz
```

Non-Linear Image Warping. Warp files describing the non-linear alignment between the raw anatomical (T1w) image and the template image generated from *fsl_anat*. No current BIDS structure exist, brainlife.io structure is as follows:

```
dt-neuro-warp.tag-preprocessed.tag-standard.id-{}
      _info.json
      inverse-warp.nii.gz
      warp.nii.gz
```

Freesurfer. Freesurfer output directory containing all derivatives generated during Freesurfer's *recon-all*. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-freesurfer.tag-preprocessed.tag-acpc_aligned.tag-hippocampal.tag-thalamic_nuclei.id-{}
      _info.json
      output
```

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Multi-Atlas Transfer Tool (MaTT). The surface and volumated mapping files of the 180 node multimodal parcellation to individual participant surfaces. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-parcellation-surface.id-{}
      _info.json
      lh.parc.annot.gii
      lh.parc.white.gii
      rh.parc.pial.gii
      key.txt
      lh.parc.inflated.gii
      rh.parc.annot.gii
      rh.parc.white.gii
      label.json
      lh.parc.pial.gii
      rh.parc.inflated.gii
dt-neuro-parcellation-volume.tag-SupraTentorial.id-{}
      _info.json
      key.txt
      label.json
      Parc.nii.gz
```

Tissue-type masks. The 5-tissue type images (GM, WM, CSF, GMWMI) used for tracking. No existing BIDS structure, brainlife.io structures is as follows:

```
dt-neuro-mask.tag-5tt_masks.id-{}
      _info.json
      csf.nii.gz
      gm.nii.gz
      wm.nii.gz
      mask.nii.gz
```

Diffusion-weighted imaging (dMRI). The final preprocessed dMRI data used for all further modeling and analyses following FSL Topup & Eddy - CUDA and MRTRix3 preproc.

```
upload/sub-{}/dwi/
      sub-{}_tag-preprocessed_tag-normalized_desc-{}_dwi.bvals
      sub-{}_tag-preprocessed_tag-normalized_desc-{}_dwi.json
      sub-{}_tag-preprocessed_tag-normalized_desc-{}_dwi.nii.gz
```

dMRI Brainmask. The final dMRI brain mask used for all modeling and analyses. No existing BIDS structure, brainlife.io structures are as follows:

```
dt-neuro-mask.tag-brain.id-{}
      _info.json
      mask.nii.gz
```

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Neurite Orientation Dispersion Density Imaging (NODDI). The neurite density, orientation dispersion, and isotropic volume fraction maps generated from NODDI AMICO. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-noddi.id-{}
      _info.json
      dir.nii.gz
      ndi.nii.gz
      odi.nii.gz
      isovf.nii.gz
```

Diffusion Tensor Imaging (DTI). The fractional anisotropy, mean diffusivity, axial diffusivity, and radial diffusivity maps generated from DTIFIT.

```
upload/sub-{}/dwi/
      sub-{}_tag-fsl_desc-{}_AD.nii.gz
      sub-{}_tag-fsl_desc-{}_GFA.nii.gz
      sub-{}_tag-fsl_desc-{}_MD.nii.gz
      sub-{}_tag-fsl_desc-{}_RD.nii.gz
```

Constrained Spherical Deconvolution (CSD). CSD models fit across L_{max}=2,4,6, and 8 using Fit Constrained Spherical Deconvolution Model For Tracking. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-csd.tag-preprocessed.id-{}/
      _info.json
      lmax2.nii.gz
      lmax4.nii.gz
      lmax6.nii.gz
      lmax8.nii.gz
      response.txt
```

Tractograms. The merged tractograms across L_{max}=6 and L_{max}=8, totaling 3 million streamlines generated from the Anatomically-constrained tractography (ACT) app.

```
upload/sub-{}/dwi/
      sub-{}_tag-merged_desc-{}_tractography.json
      sub-{}_tag-merged_desc-{}_tractography.tck
```

White Matter Anatomy (wma) Segmentation. Major track segmentation generated from White Matter Anatomy Segmentation. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-wmc.id-{}
      _info.json
      classification.mat
      surfaces
      tracts
```

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Segmentation Cleaned. The cleaned tracks from Remove Fiber Outliers. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-wmc.tag-cleaned.id-{}
      _info.json
      classification.mat
      output_fibercounts.txt
      tracts
```

Tract Profiles. Mapping of DTI and NODDI metrics along the core of the segmented white matter tracts using the Tract Analysis Profiles app. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-tractprofile.id-{}
      _info.json
      profiles
```

Network Generation. Network adjacency matrices were generated using the Structural Connectome MRTrix3 (SCMRT) (SIFT2) app. No existing BIDS structure, brainlife.io structure as follows:

```
dt-raw.tag-networkmatrices.id-{}
      _info.json
      output
```

Cortical DTI and NODDI mapping. Surfaces and DTI and NODDI measure files mapped to the surface generated from Cortical Tissue Mapping. No existing BIDS structure, brainlife.io structure is as follows:

```
dt-neuro-cortexmap.id-{}
      _info.json
      cortexmap
            Func
            Label
            surf
```

Technical Validation

In this section, we provide a qualitative evaluation of the data derivatives made available on brainlife.io. We provide qualitative analysis of the preprocessing of the anatomical (T1w) image, including the seed mask, and pial and white matter surfaces generated from Freesurfer. Qualitative images of the dMRI preprocessing, dMRI modeling (CSD and NODDI), dMRI tractography, network generation, and mapping of diffusion measures to the cortical surface are also provided. We further provide a quantitative analysis of the SNR of the dMRI data following preprocessing.

Anatomical (T1w) preprocessing.
Anatomical (T1w) images were *linearly* aligned to the MNI152 0.8 mm template and further segmented into gray-matter, white-matter, CSF, and gray- and white-matter interface masks using brainlife.app.273. See **Methods: Anatomical (T1w) preprocessing** for more details. Each participant's aligned anatomical images (T1w), and all derivatives generated from the aligned images, are provided.

Figure 1a exemplifies the quality of the linear alignment obtained with brainlife.app.300 in representative participants from each athlete group (i.e. Football: *top*, Cross-Country: *middle*, and Non-Athlete: *bottom*). The gray-

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and white-matter interface mask (1b) and white matter boundary (1c) are overlaid on the 'acpc-aligned' anatomical (T1w) image to further provide quality assurance. These images were generated with brainlife.app.312.

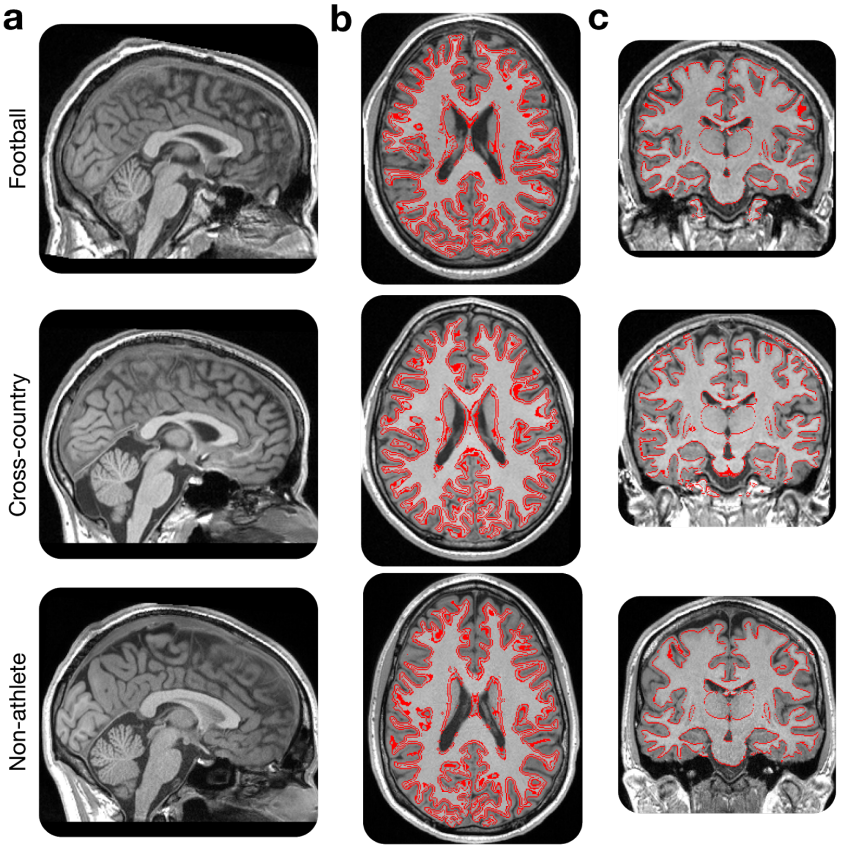

Figure 1. Anatomical (T1w) preprocessing: Alignment and segmentation. Representative mid-plane images from each group of the preprocessed anatomical (T1w) image. (a) Sagittal slice of MNI152 (ACPC) aligned T1 used for all subsequent preprocessing, (b) Axial slice with gray - and white-matter interface outlined (red) used as a seed mask for tractography, and (c) Coronal slice with white-matter boundary outlined (red). Images were generated using brainlife.app.300 and brainlife.app.312

Following alignment and segmentation, Freesurfer was used to generate cortical and white matter surfaces, along with the Destrieux Atlas parcellation using brainlife.app.0. Figure 2a demonstrates the quality of the surface generation representative participants from each athlete group (i.e. Football: *top*, Cross-Country: *middle*, and Non-Athlete: *bottom*). Images of the Destrieux (aparc.a2009s) atlas (Destrieux et al., 2010) on the pial surface, along with images of the pial and white matter surface outlines overlaid on the 'acpc-aligned' anatomical (T1w) image, are provided as a means of quality assurance. Figure 2b illustrates the mapping of the 180 node multimodal atlas (Glasser et al., 2016) to representative participants from each group mapped using brainlife.app.23. These images were generated using brainlife.io's Freeview and Connectome Workbench viewers.

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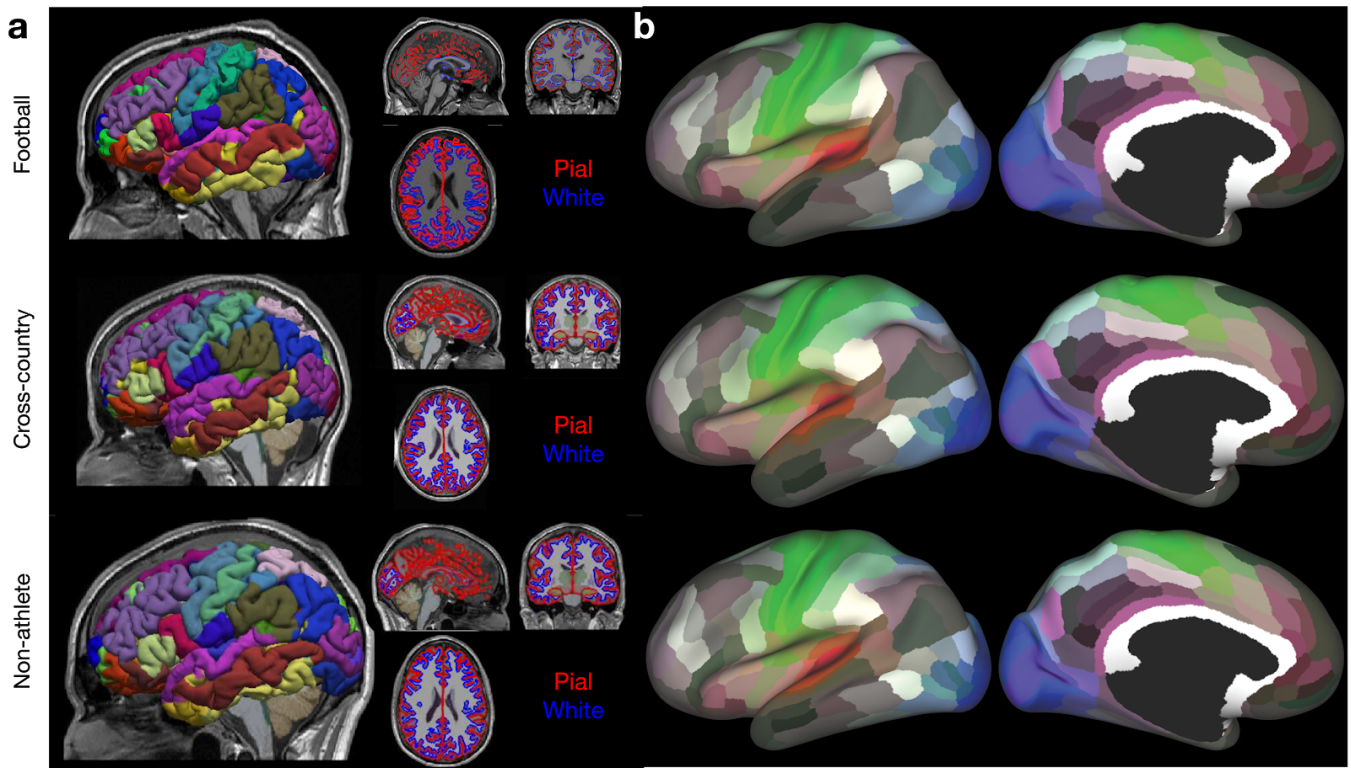

Figure 2. Anatomical (T1w) preprocessing: Freesurfer and 180 node multimodal atlas mapping a. Representative images from each group of the Freesurfer outputs: pial (*red*) and white (*blue*) matter surfaces, and the aparc.a2009s+aseg (i.e. Destrieux) parcellation. Images were generated using brainlife.io's Freeview viewer. **b.** Representative images from each group of the 180-node multimodal (hcp-mmp) atlas mapped to an inflated representation of the cortical surface. Images were generated using brainlife.io's Connectome Workbench viewer.

Diffusion (dMRI) preprocessing.
Raw dMRI images were corrected for susceptibility-weighting, eddy currents, motion, biasing, and Rician background noise using a combination of methods. Following preprocessing, the dMRI images were aligned to the 'acpc-aligned' anatomical (T1w) image. See **Methods: Diffusion (dMRI) preprocessing** for more details. The preprocessing was performed using brainlife.app.287 and brainlife.app.68. Following preprocessing, the signal-to-noise ratio (SNR) was computed for each subject in the non-diffusion weighted volumes (i.e. b=0) and the diffusion-weighted volumes (i.e. b=1000,2000) separately as a means for quality assurance. The SNR was computed using brainlife.app.120.

Figure 3a demonstrates the quality of alignment of the dMRI and 'acpc-aligned' anatomical (T1w) image from representative participants from each group. The fractional anisotropy (FA) map (see **Methods: White matter microstructure: DTI** for more details on DTI fitting) from each subject is overlaid in red-yellow on the 'acpc-aligned' anatomical (T1w) images. Overall, the alignments of the dMRI and the anatomical image are anatomically-sound. The fully preprocessed dMRI images from each participant, along with their corrected b-vectors and b-values, are provided. The images were generated using brainlife.app.309. Figure 3b documents the non-diffusion weighted and diffusion-weighted SNRs for each participant. The average SNR for Football players (*orange*) following preprocessing was 25.839 for non-diffusion weighted volumes (SD = ± 5.236). This was slightly lower than the SNR for Cross-country runners (*pink*) with an average SNR in the non-diffusion weighted volumes of 33.1078 (SD = ± 4.399). Non-athletes overall had the lowest average SNR in the non-diffusion weighted volumes (21.918, SD = ± 6.867).

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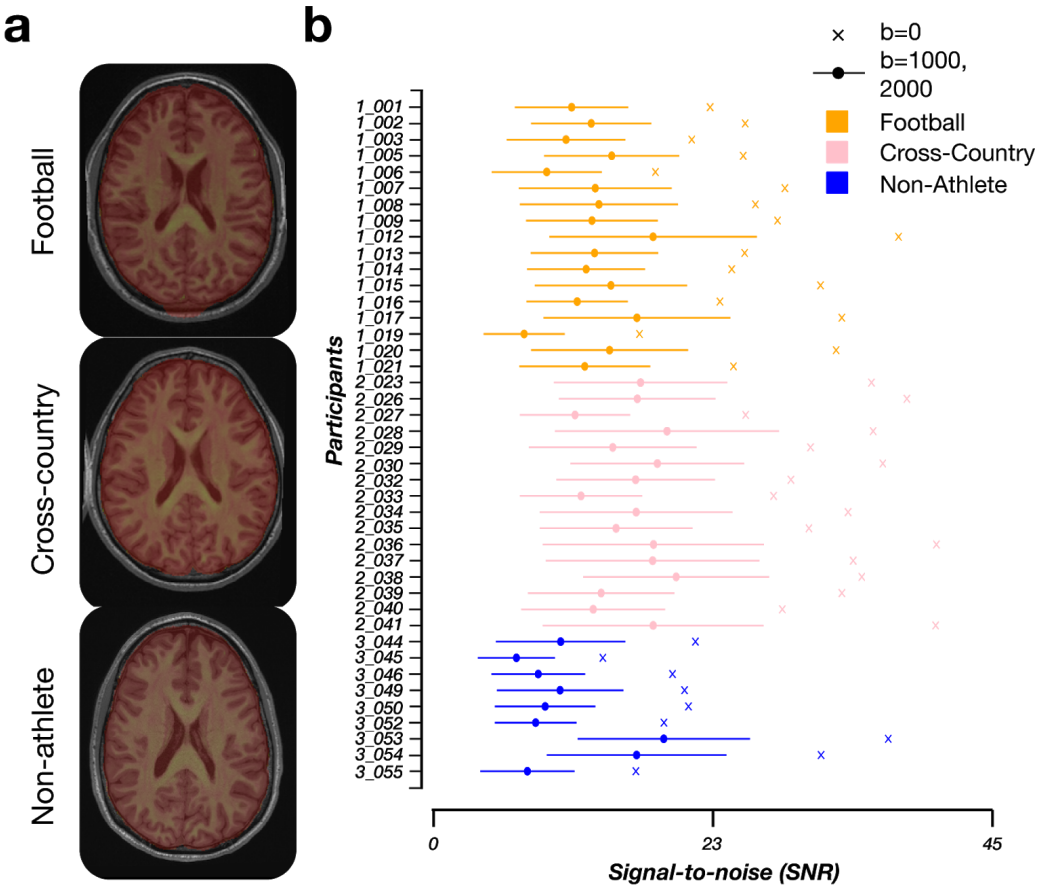

Figure 3. Qualitative and quantitative quality-assurance measures following dMRI preprocessing. a. Representative mid-axial images of the fractional anisotropy (FA) (*red-yellow*) image overlaid on the 'acpc aligned' anatomical (T1w) image. Images were generated using brainlife.app.309. **b.** The signal-to-noise ratio for each participant from each group (football: *orange*, cross-country: *pink*, non-athlete: *blue*) following dMRI preprocessing. The average SNR was computed in the Corpus Callosum across the b=0 shells (*crosses*) and b=1000,2000 shells (*circles*). Standard deviation across the non-b=0 shells are plotted as error bars for each participant.

White matter microstructure modeling: DTI and NODDI.
Following preprocessing, models of microstructure were fit to the dMRI images. Specifically, the diffusion tensor (DTI) and neurite orientation dispersion density imaging (NODDI) models were fit to the b=1000 and b=1000, 2000 shells respectively. See **Methods: White matter microstructural modeling: DTI & NODDI** for more details. DTI was fit using brainlife.app.292, while NODDI was fit using brainlife.app.365. The DTI and NODDI maps for each participant are provided. Figure 4 demonstrates the quality of fit of both the DTI and NODDI models on representative participants from each group. Specifically, mid-axial slices of the fractional anisotropy (FA),mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD) from the DTI model, and the orientation dispersion and neurite density indices (ODI, NDI) and the isotropic volume fraction (ISOVF) from the NODDI model are presented. There is a high anatomical correspondence between the measures and known anatomical properties. For example, the ventricles across all three participants are saturated in the MD maps, as water moves maximally isotropically. In the white matter, FA and NDI are highest in the highest concentrations of white matter, while ODI is lowest. The images were generated using brainlife.app.302 and brainlife.app.367.

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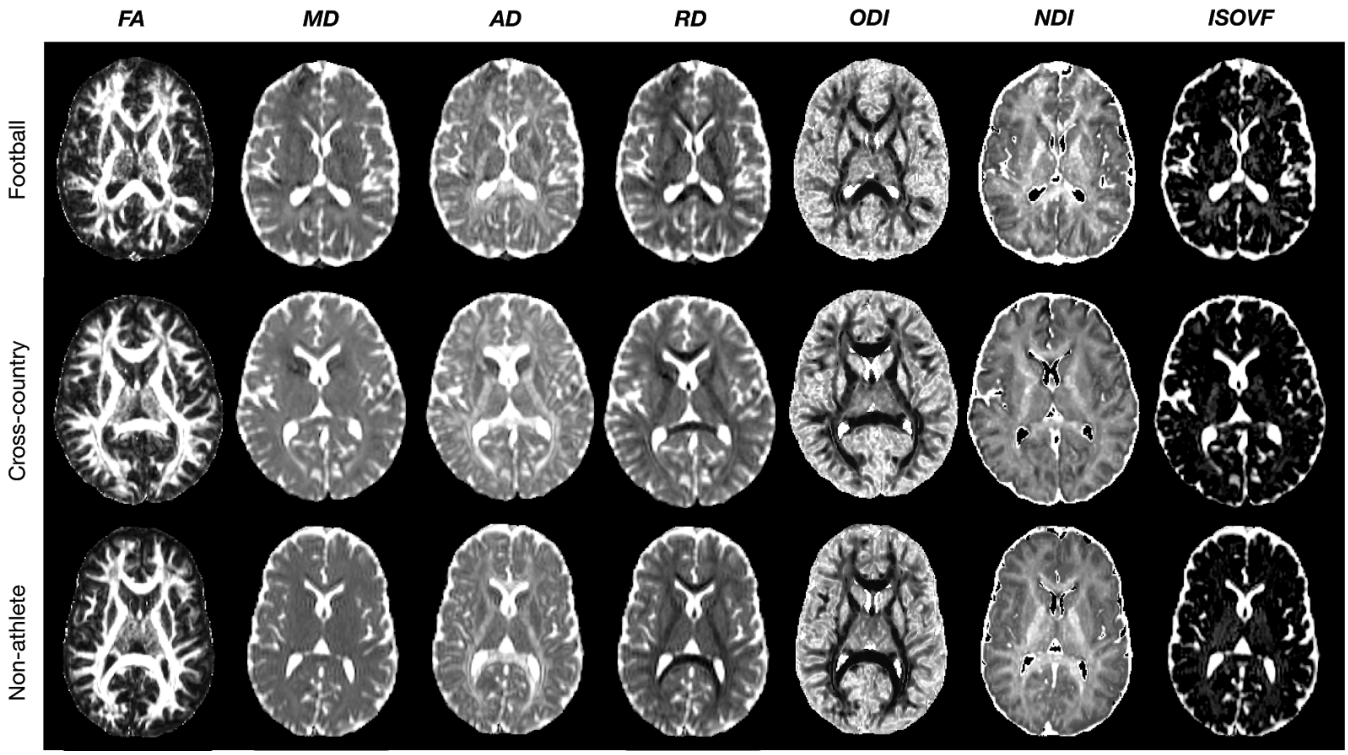

Figure 4. dMRI Modelling: DTI and NODDI. Qualitative quality-assurance figures following fitting of the Diffusion Tensor (DTI) and Neurite Orientation Dispersion Density Imaging (NODDI) models. (a) Representative mid-axial images of the fractional anisotropy (*FA*), mean diffusivity (*MD*), axial diffusivity (*AD*), radial diffusivity (*RD*), orientation dispersion index (*ODI*), neurite density index (*NDI*), and isotropic volume fraction (*ISOVF*). Images were generated with brainlife.app.302 and brainlife.app.367.

White matter microstructural modeling: CSD.

In order to map white matter macrostructure via white matter tractography, the constrained spherical deconvolution model (CSD) was fit to each participant across 4 maximum spherical harmonic orders (i.e. L_{max}): 2,4,6 and 8. L_{max}=6,8 were chosen for tracking. See **Methods: White matter microstructural modeling (CSD)** for more details. The CSD was fit using brainlife.app.238. Each participant's CSD fits across all four L_{max}'s are provided. Figure 5 demonstrates the quality of fit of the CSD model on representative participants from each group using L_{max}=8. In the left column, the response function generated is mapped to a sphere, while the right column corresponds to the fiber orientation dispersion function (fODF). The response functions demonstrate a quality fit due to the relatively flat shape and sharp folding in the center. In the fODF maps, clear anatomy is distinguished in regions of the highest white matter concentration. Images were generated using brainlife.app.311 and brainlife.app.317.

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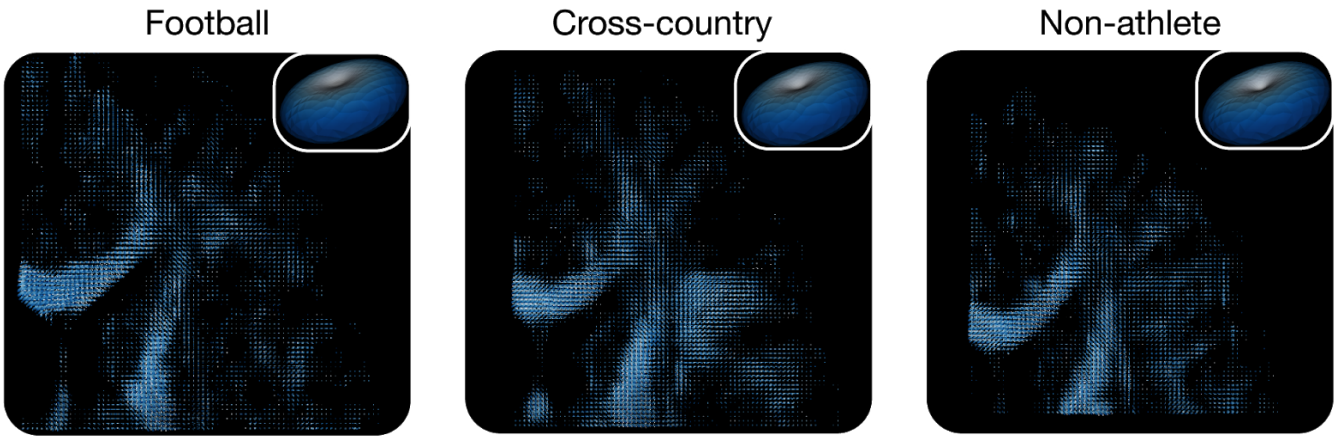

Figure 5. dMRI Modelling: Constrained Spherical Deconvolution. Example outputs of the fiber orientation dispersion function (fODF) for maximum spherical harmonic order (L_{max}) of 8 and the csd response functions (*inset*). Images were generated using brainlife.app.311 and brainlife.app.317.

White matter microstructure modeling: Anatomically-constrained tractography

Following the fitting of the CSD model to each participant, anatomically-constrained tractography (ACT) was performed on L_{max}=6,8 to generate whole-brain tractograms containing 3 million streamlines. These tractograms were used for subsequent segmentation and network generation. See **Methods: White matter microstructure modeling (Tractography)** for more details. The tractograms were generated using brainlife.app.297, and merged using brainlife.app.305. Each participant's whole-brain tractogram containing 3 million streamlines per tractogram is provided. Figure 6a demonstrates the quality of the tractography in representative participants from each group. The whole-brain tractogram of each participant shows high densities of streamlines filling the entire brain volume, as expected. The images were generated using brainlife.app.310.

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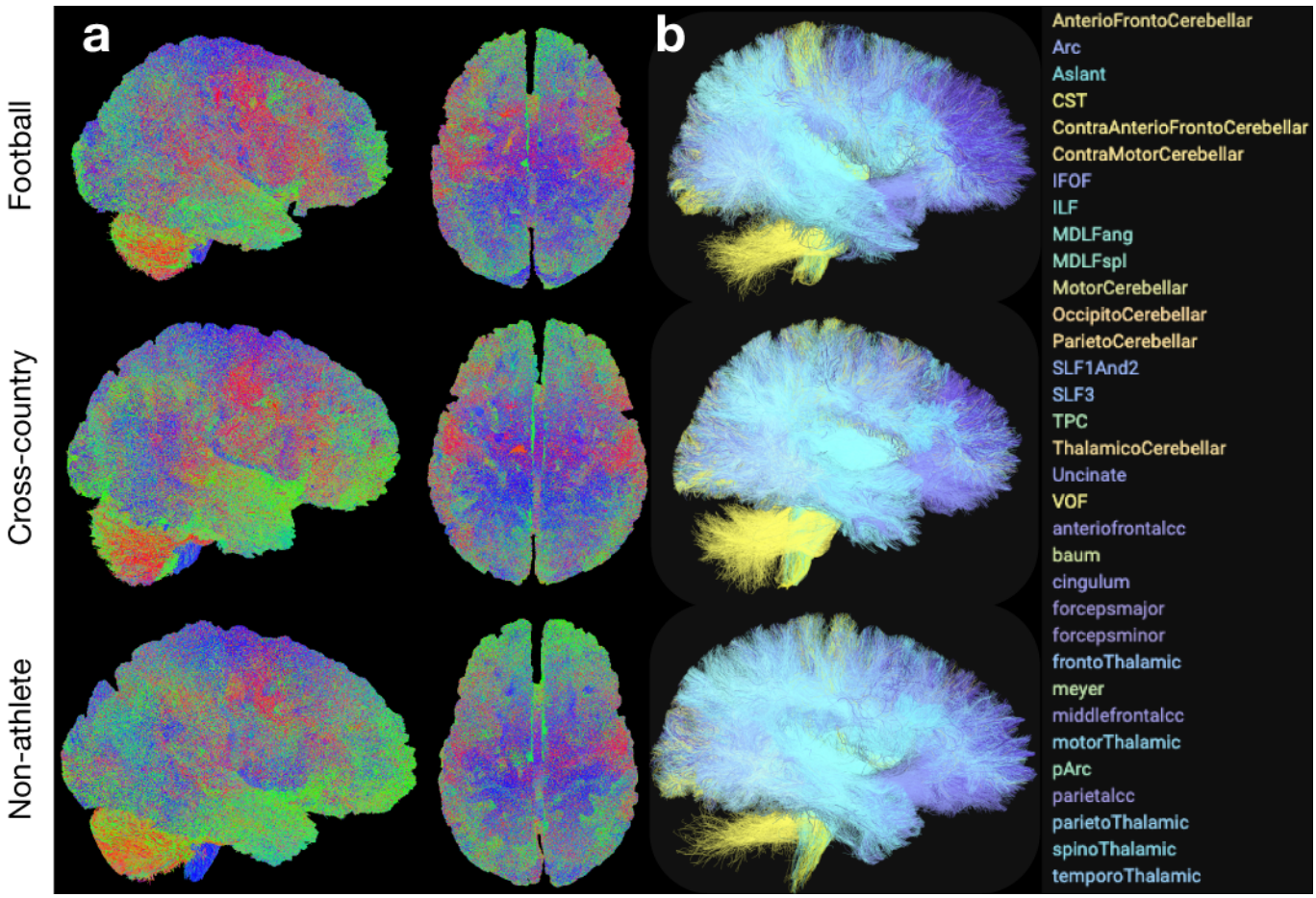

Figure 6. Ensemble Tractography. a. Example tractogram from each group subsampled from the 'merged' 3 million streamline tractogram (50k streamlines sampled per tractogram). The images were generated using brainlife.app.310. **b.** Example cleaned segmentation from each group. The images were generated using brainlife.io's tract segmentation viewer.

White matter microstructure modeling: Segmentation and cleaning

Following tractography, each participant's whole-brain tractogram was segmented using a recently published methodology using anatomical definitions of common white matter tracts. In brief, this segmentation classifies streamlines as belonging to a particular tract based on their cortical terminations and known shape characteristics. See **Methods: White matter microstructure modeling (Segmentation & Cleaning)** for more details. Tract segmentation was performed using brainlife.app.188. Following segmentation, each tract was cleaned by removing outlier streamlines using brainlife.app.195. Each participant's segmentation, both cleaned and uncleaned, is provided. **Figure 6b** provides representative white matter tract segmentation from participants from each group. From a qualitative perspective, each segmentation fills the whole-brain volume and contains a relatively high density of streamlines per tract. Each of the tracts is listed on the right. The images were generated using the brainlife.io tract segmentation viewer.

White matter microstructure modeling: Tract profiles

Following white matter tract segmentation and cleaning, tract profilometry (Yeatman et al., 2012) was performed for each participant and each tract. In brief, a central representation (i.e. 'core') of each tract was computed by weighted-average of the X,Y, and Z coordinates of all the streamlines in the tract. Streamlines were then resampled to 200 equally spaced nodes, and the average microstructural measures (DTI, NODDI) were computed at each node. The first and last ten nodes were removed, and then the profiles for each tract were averaged across each

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group. See **Methods: White matter microstructure modeling (Tract profiles)** for more details. Tract profiles were computed using brainlife.app.361. Tract profilometry data for all participants and tracts are provided. **Figure 7a** provides a representative Right ILF from a Football player. **Figure 7b** illustrates the centralized core of the ILF and the ODI values mapped along the tract. **Figure 7c** provides the group average ODI and FA tract profiles for the Right ILF. These profiles document the ability of this methodology for identifying group differences along a tract. Images were generated using the Matlab Brain Anatomy toolbox https://github.com/francopestilli/mba(Pestilli et al., 2014) scripts available at https://github.com/bacaron/athlete-brain-study.

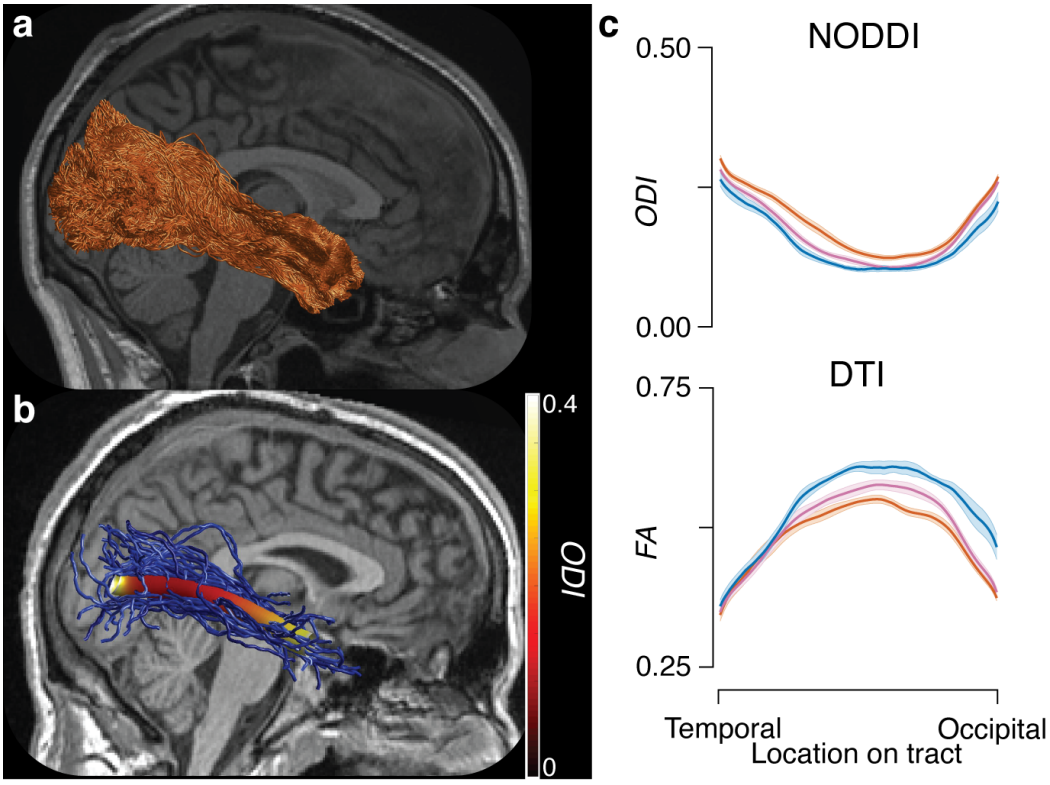

Figure 7. Tract Profiles. a. Example of a segmented Right ILF tract from a representative Football player. **b.** Example of the centralized 'core' representation of the Right ILF in the same subject as in **a**, with ODI mapped along the 'core'. **c.** Group average tract profiles for ODI (*top*) and FA (*bottom*) for the Right ILF (orange: football players, pink: cross-country runners; blue: non-athletes; error bars ±1 SE.) Images were generated using the Matlab Brain Anatomy toolbox https://github.com/francopestilli/mba(Pestilli et al., 2014) scripts available at https://github.com/bacaron/athlete-brain-study.

White matter microstructure modeling: Network adjacency matrix generation

The whole-brain tractograms from each participant were used to generate structural connectomes. Specifically, measures of streamline count and density are computed between each node in the multimodal 180 cortical node parcellation and network matrices are generated. See **Methods: White matter microstructure modeling (Network generation)** for more details. Network adjacency matrices were generated using brainlife.app.394. **Figure 8** demonstrates group average connectivity matrices using log streamline count, log density, and average FA across the streamlines connecting nodes from each group and the total dataset. Images were generated using the *imagesc* function in MATLAB.

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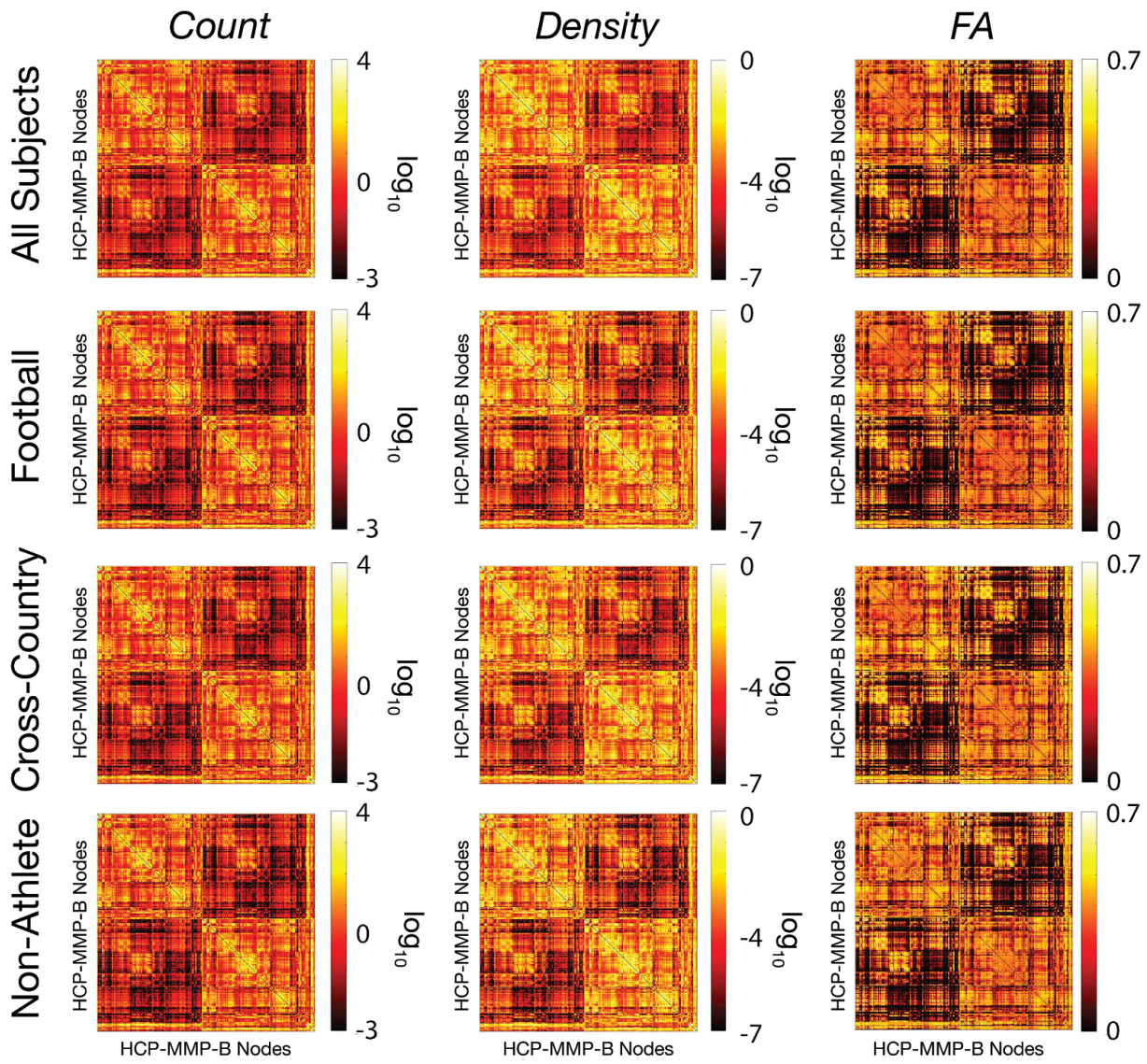

Figure 8. Average structural connectivity matrices. Twelve representative matrices of connectivity between brain regions defined in the 180 multimodal cortical atlas(Glasser et al., 2016) (i.e. HCP-MMP). Adjacency matrices average streamline (*left*), density (*middle*), and FA (*right*) averaged across all subjects (*top*), football players (*2nd row*), cross-country runners (*3rd row*), and non-athlete students (*4th row*). Images were generated using *imagesc* in MATLAB.

Cortical white matter microstructure mapping.
Diffusion-based measures of microstructure were also mapped to a surface representation of the midthickness (i.e., the average coordinates between pial and white matter boundary surface; (Fukutomi et al., 2018)), here after simply referred to as 'cortical,' or 'cortical.' For more details on the differences between the two mappings, see **Methods: White matter microstructural modeling: DTI & NODDI**. The DTI and NODDI maps for each participant for the cortical white matter mapping analyses are provided as well. These measures were then mapped to the cortex following the procedures described in Fukutomi et al 2018 (Fukutomi et al., 2018). See **Methods: Cortical white matter microstructure mapping** for more details. Diffusion measures were mapped using brainlife.app.379. Figure 8 demonstrates the quality of fit of DTI and NODDI measures on the cortical surface. Specifically, the FA and ODI maps mapped to a representative participant's cortical surface. Anatomic landmarks, including higher FA and lower

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ODI in motor and somatosensory cortices, are consistent across participants and map well to the results presented in Fukutomi et al 2018. These images were generated using brainlife.io's Connectome Workbench viewer.

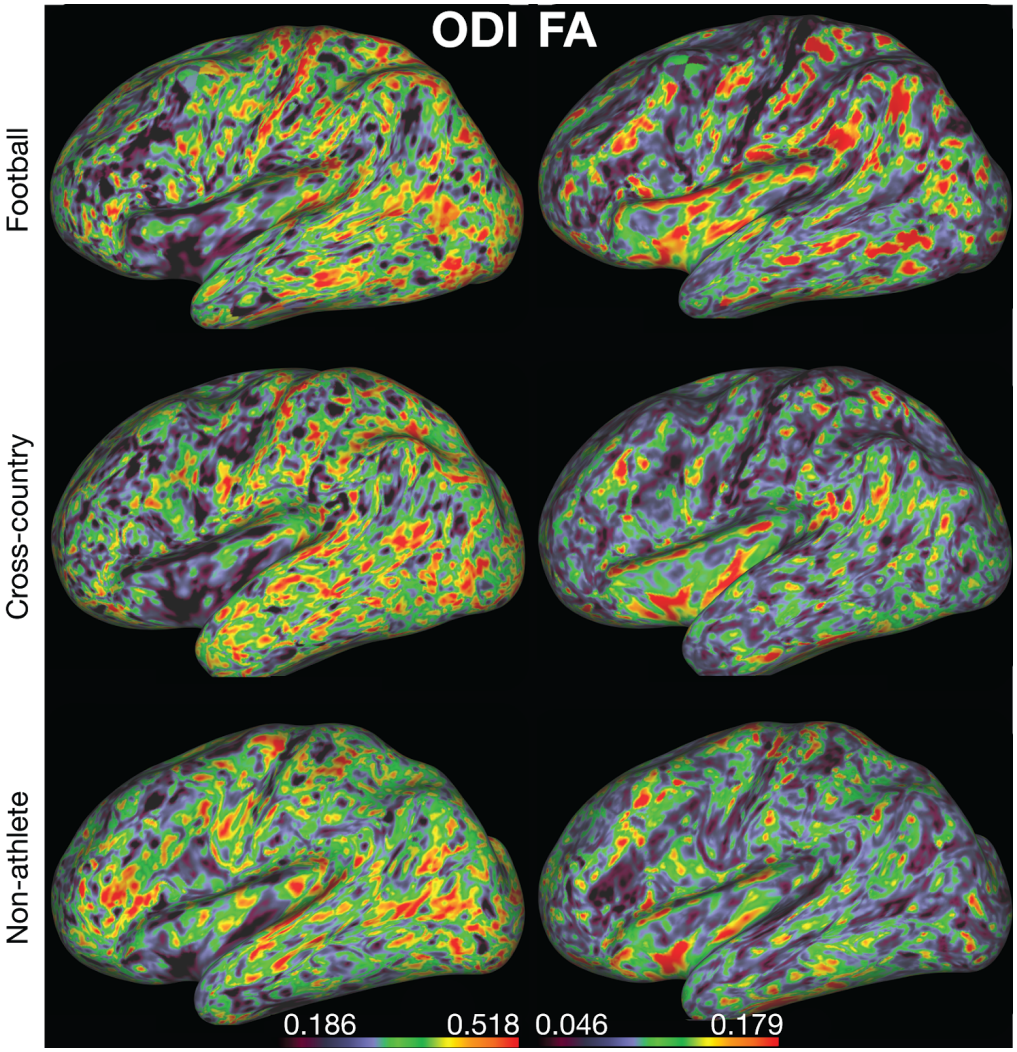

Figure 9. Surface-based mapping of microstructural white matter. Example ODI (left) and FA (right) estimates mapped to the cortical surface for a representative participant in each group (football: top, cross-country: middle, non-athlete: bottom). These images were generated using brainlife.io's Connectome Workbench viewer.

Usage Notes

The data are available on brainlife.io. Data files can be downloaded, and some can be organized into BIDS standard (Gorgolewski et al., 2016). The data derivatives are stored in numerous formats, including NIFTI, TCK, GIFTI, and .mat. Access to the published data is currently supported via (i) web interface and (ii) Command Line Interface (CLI).

The brainlife.io CLI can be installed on most Unix/Linux systems using the following command:

```
npm install brainlife.io -g.
```

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The CLI can be used to query and download partial or full datasets. The following example shows the CLI command to download all T1w datasets from a subject in the publication data:

```
bl pub query # this will return the publication IDs
bl bids download --pub <insert pub id> --subject 1_001 --datatype \
neuro/anat/t1w --tag "fsl_anat"
```

The following command downloads the data in the entire project (from Release 1) into BIDS format:

```
bl bids download --pub 5f2c3765beafe924c962dd8d
```

Additional information about the brainlife.io CLI commands can be found at https://github.com/brainlife/cli.

Code availability

Table 1 below reports the links to each web service and github.com URL implementing the processing pipeline. All code not found on brainlife.io, including visualization code, can be found at https://github.com/bacaron/athlete-brain-study.

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