ADNI Alzheimer's Disease Neuroimaging Initiative

Diffusion Tensor Imaging Summary Statistics of White Matter Regions of Interest

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Contents

Summary (or Abstract)

Diffusion tensor imaging (DTI) allows for study of the microstructural properties of white matter tracts. Regional summary measures were calculated from DTI to include measures of diffusion and anisotropy of various fiber tracts within the brain. A standard DTI- template, with a corresponding white matter tract atlas, was registered to each individual subject. Registrations were subsequently applied to the segmented atlas. Visual inspection of the images ensured adequate registration. The mean of all voxels from each of the regions of interest from the atlas were obtained from maps of fraction (FA), mean diffusivity (MD), radial diffusivity (RD), and axial diffusivity (AD).

Method

Processing methods for obtaining summary statistics in white matter regions of interest are described below.

Preprcoessing Steps

For each subject, all raw DWI volumes were aligned to the average b_0 image (DTI volume with no diffusion sensitization) using the FSL *eddy-correct* tool (www.fmrib.ox.ac.uk/fsl) to correct for head motion and eddy current distortions. All extra-cerebral tissue was roughly removed from the T1-weighted anatomical scans using a number of software packages, primarily ROBEX, a robust automated brain extraction program trained on manually "skull-stripped" MRI data from (Iglesias et al., 2011) and Freesurfer (Fischl et al., 2004). The resulting skull stripped volumes were visually inspected, and the best one selected and sometimes further manually edited. Anatomical scans subsequently underwent intensity inhomogeneity normalization using the MNI *nu_correct* tool (www.bic.mni.mcgill.ca/software/). Non-brain tissue was also removed from the diffusion-weighted images using the Brain Extraction Tool (BET) from FSL (Smith, 2002).

To align data from different subjects into the same 3D coordinate space, each T1-weighted anatomical image was linearly aligned to a version of the Colins27 brain template (Holmes et al., 1998) using FSL's *flirt* (Jenkinson et al., 2002) with 6 degrees of freedom to allow translations and rotations in 3D. The Colin27 brain was zero-padded to have a cubic

isotropic image size (220x220x220 1mm^3) and then downsampled (110x110x110 2mm^3) to be more similar to the DWI resolution.

To correct for echo-planar imaging (EPI) induced susceptibility artifacts, which can cause distortions at tissue-fluid interfaces, skull-stripped b_0 images were linearly aligned to their respective T1-weighted structural scans using FSL's *flirt* with 9 degrees of freedom, and then elastically registered to their aligned T1 scans using an inverse consistent registration algorithm with a mutual information cost function (Leow et al., 2007) as described in (Jahanshad et al., 2010). The resulting 3D deformation fields were then applied to the remaining 41 DWI volumes prior to mapping diffusion parameters. To account for linearly registering the average b0 from the DWI images to the structural T1-weighted scan, a corrected gradient table was calculated

DTI maps

A single diffusion tensor (Basser et al., 1994) was modeled at each voxel in the brain from the eddy- and EPI-corrected DWI scans using FSL's *dtifit* command, and scalar anisotropy and diffusivity maps were obtained from the resulting diffusion tensor eigenvalues (λ_1, λ_2, λ_3). Fractional anisotropy (FA), was calculated from the standard formula:

$$FA = \sqrt{\frac{3}{2}} \frac{\sqrt{(\lambda_1 - <\lambda>)^2 + (\lambda_2 - <\lambda>)^2 + (\lambda_3 - <\lambda>)^2}}{\sqrt{\lambda_1^2 + \lambda_2^2 + \lambda_3^2}} \quad \in [0,1]$$

$$<\lambda> = \frac{\lambda_1 + \lambda_2 + \lambda_3}{3}$$

-where $<\lambda>$ is the mean diffusivity (MD). Radial diffusivity (RD), was calculated as the average of the two smallest eigenvalues:

$$RD = \frac{\lambda_2 + \lambda_3}{2}$$

Axial diffusivity was defined as the primary (largest) eigenvalue (AD=λ_1).

White matter tract atlas ROI Summary measures

We registered the FA image from the JHU DTI atlas (Mori et al., 2008) to each subject using a previously described mutual information based elastic registration algorithm (Leow et al., 2007). We then applied the deformation to the stereotaxic JHU "Eve" WM atlas labels (http://cmrm.med.jhmi.edu/cmrm/atlas/human_data/file/AtlasExplanation2.htm) using nearest neighbor interpolation to avoid intermixing of labels. This placed the atlas ROIs in the same coordinate space as our DTI maps. We were then able to calculate the average FA, MD, RD, and AD within the boundaries of each of the ROI masks for each subject (**Table I**). Of the 56 WM ROIs, we excluded 4 ROIs, the left and right middle cerebellar peduncle and pontine crossing tract, as they often time fall partially or completely out of the field of view (FOV). We note that this is also occasionally true of the left and right medial lemniscus, inferior and superior peduncles. We only included non-zero voxels within the FOV in our calculations of mean FA and diffusivity measures. In addition to the 52 JHU labels, 5 more ROIs were evaluated: the bilateral fornix, bilateral genu, bilateral body and bilateral splenium of the corpus callosum, as well as the full corpus callosum, to get full summary measures of these regions.

Table I. Index of JHU "Eve" WM atlas labels (http://cmrm.med.jhmi.edu/cmrm/atlas/human_data/file/AtlasExplanation2.htm) from which summary ROI FA, MD, RD, and AD measures were calculated.

ROI	Hemisphere	Notes:
Corticospinal tract	left, right	
Inferior cerebellar peduncle	left, right	
Medial lemniscus	left, right	
Superior cerebellar peduncle	left, right	
Cerebral peduncle	left, right	
Anterior limb of internal capsule	left, right	
Posterior limb of internal capsule	left, right	
Posterior thalamic radiation	left, right	includes optic radiation
Anterior corona radiata	left, right	
Superior corona radiata	left, right	
Posterior corona radiata	left, right	
Cingulum	left, right	cingulate gyrus
Cingulum (hippocampus)	left, right	
Fornix (cres) / Stria terminalis	left, right	can not be resolved with current resolution
Superior longitudinal fasciculus	left, right	
Superior fronto-occipital fasciculus	left, right	could be a part of anterior internal capsule
Inferior fronto-occipital fasciculus	left, right	
Sagittal stratum	left, right	includes inferior longitudinal fasciculus and inferior fronto-occipital fasciculus
External capsule	left, right	
Uncinate fasciculus	left, right	
Fornix	left, right	column and body of fornix
Genu of corpus callosum	left, right	
Body of corpus callosum	left, right	
Splenium of corpus callosum	left, right	
Retrolenticular part of internal capsule	left, right	
Tapatum	left, right	
Bilateral genu of the corpus callosum	average left and right	
Bilateral body of the corpus callosum	average left and right	
Bilateral splenium of the corpus callosum	average left and right	
Bilateral full corpus callosum	average genu, body splenium	
Bilateral fornix	sum left and right	

TBSS tract atlas ROI Summary measures

Tensor based spatial statistics (TBSS; Smith et al., 2006) was also performed and the mean FA in regions of interest along the skeleton were extracted. TBSS was performed according to protocols outlined by the ENIGMA-DTI group: http://enigma.loni.ucla.edu/wp-content/uploads/2012/06/ENIGMA_TBSS_protocol.pdf

In short, all subjects were registered to the ENIGMA-DTI template in ICBM space and standard *tbss* steps were performed to project individual FA maps onto the skeletonized ENIGMA-DTI template. ROI extraction was also performed according to the following protocol

to extract the mean FA in ROIs along the skeleton: http://enigma.loni.ucla.edu/wp-content/uploads/2012/06/ENIGMA_ROI_protocol.pdf.

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