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A Diffusion MRI Resource of 80 Age-varied Subjects with Neuropsychological and Demographic Measures

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Intended Audience: Researchers studying aging and cognition using diffusion MRI of the human brain or developing computational methods for such.
Purpose: The primary purpose of this work is to provide a resource of high angular resolution diffusion MRI datasets of 80 normal volunteers aged 25-64 together with neuropsychological testing data spanning general cognitive ability, memory, and information processing speed. To support the value of these data, we demonstrate statistical correlations between age and tract-based metrics calculated automatically from the data. The metrics are a function of fiber count, length, diffusion rate, and diffusion anisotropy; the statistical relationship to age was modeled with linear regression.
Methods: Participants were 80 (39 male) healthy volunteers aged 25 to 64 years (mean=43.0, SD=10.5 years) who were enrolled in an IRB-approved protocol. MRI was conducted on a GE 1.5 T clinical scanner and included a T1-weighted volume (1x1x1.3mm, resolution 256x256x120) and dMRI protocol (2x2x2mm, 64-direction, b=1000s/mm^2, resolution 128x128x72). Each dMRI volume was corrected for subject motion and eddy current artifacts by affine registration to the first T2-weighted (b=0 s/mm^2) volume. All registrations were performed with FSL 5.0's FLIRT with mutual information [1]. The orientations of the b-vectors were corrected by the rotation induced by these registrations, while brain extraction was performed using FSL's BET. Deterministic tractography was performed with custom software. Diffusion tensors were fit from the linearly interpolated dMRI volumes, and the principal eigenvector was used for tracking with one random seed per voxel, second-order Runge-Kutta integration, an angle threshold of 35^0, an FA threshold of 0.15, and a minimum length of 10 mm. The T1 volume was segmented into gray matter areas using Freesurfer 5.1.0 [2], and regions from the Desikan-Killiany atlas were grouped into lobular structures. For each subject, fibers were mapped to the T1 space by rigid alignment with the FA volume. The fibers were similarly mapped to the JHU white matter atlas [3]. Following this, we performed segmentation using custom software. We performed connectivity-based segmentation with the lobular regions, including four lobe areas and the subcortex for each hemisphere (10 regions in total). For each pair of regions, a bundle was created from fibers with endpoints within one voxel of the regions. We found 30 pairs of regions with fibers present in all subjects. We also performed tract-based segmentation using the maximum probability threshold of each of 16 tracts in the JHU atlas. For each tract, bundles were created from fibers with at least 80% of their arc length contained by the mask. For both bundle types, fibers were culled by removing random fibers within a distance of 0.8 mm of an existing fiber. [4] For each fiber, the length and mean tensor indices (FA and MD) were computed by numerical integration along the curve. For each bundle, we determined the mean and summed tensor indices (as well as length-weighted versions), mean and summed fiber length, and fiber count (11 metrics in total). [5] Finally, we modeled the statistical relationship between each of the metrics and age, including sex as a covariate, using linear regression with the 'lm' function in R 2.15.1 [6]. We tested the hypothesis that each age regression coefficient was non-zero, and false discovery rate correction was used to control for multiple comparison within each bundle type.
Results: For both bundle types, we found significant changes ($p<0.05$) with age after correction for multiple comparisons, as indicated in the tables below. Most decreases in white matter integrity were found in frontal fibers. Sum-based metrics were more numerous than mean-based metrics, and weighted metrics were slightly more numerous than non-weighted. FA and MD effects were present in roughly equal numbers. We found both increasing and decreasing trends in the metrics with age, as reported by the sign of the regression coefficient beta in the tables below.
Discussion and Conclusions: Previous work has found age effects in frontal white matter [8,9] that are similar to our results; however, few studies have incorporated tractography statistics such as fiber length weighting and sum metrics, which we found to be sensitive to changes with age. As a resource, a significant value of this dataset is the opportunity to use it in studying both aging and methods for analysis of diffusion MRI data. We present only a tensor-based first step that supports the value of the data. There are many potential hypothesis-driven and exploratory analyses of the relationship between these images, aging, and neuropsychological data. This resource also provides an opportunity to develop, test, and compare dMRI analysis methods, including alternate diffusion models, tractography algorithms, and visualization methods. The dataset is available by request from our group website [10].
References: [1] Jenkinson et al NeuroImage 2012, [2] Dale et al NeuroImage 1999, [3] Wakana et al Radiology January 2004, [4] Zhang et al Trans. Vis. and Comp. Graph. 2003, [5] Correia et al NeuroImage 2008, [6] http://www.R-project.org, [7] Jianu et al ISMRM 2012, [8] Salat et al Neurobiology of Aging 2005, [9] Davis et al NeuroImage 1999, [10] http://vis.cs.brown.edu/downloads

Tract	Beta	Significant Metrics
FM	(-)	Sum FA, Sum Length, Sum wFA, Num
UF-L	(+)	Sum MD, Sum wMD, Num
ILF-L	(+)	Sum wMD, Sum Length, Num
CST-L	(+)	Mean wFA, Mean Length
CH-R	(+)	Mean Length

Table 1: Significant effects in age in tract-based bundles. Key: FM=forceps minor, UF=uncinate fasciculus, ILF=inferior longitudinal fasciculus, CST=corticospinal tract, CH=cingulum (hippocampal part), -L=left, -R=right, w=length weighted, FA=fractional anisotropy, MD=mean diffusivity

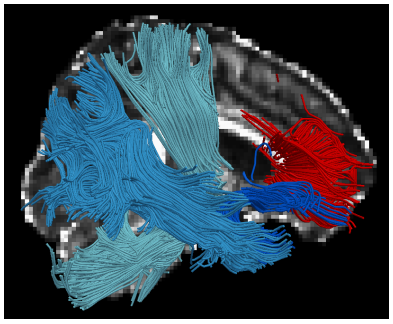

Figure 1: Significant effects with age in tract-based bundles. Red and blue indicate negative and positive correlation, respectively. Example fibers from a single subject are shown, including the forceps minor, left uncinate fasciculus, left cortical spinal tract, and left inferior longitudinal fasciculus.

Pair	Beta	Significant Metrics
SL-SR	(+)	Mean wFA, Mean wMD, Sum wMD, Mean Length
PL-PR	(-)	Sum FA, Sum Length, Num
FL-FR	(-)	Sum Length, Num
FR-SR	(-)	Sum Length, Num
SL-FR	(+)	Sum MD, Sum wMD
PL-FR	(-)	Num
FL-SL	(-)	Num

Table 2: Significant effects in age in connectivity-based bundles. Key: L=left, R=right, F=frontal, T=temporal, P=parietal, O=occipital, S=subcortical, w=length weighted, FA=fractional anisotropy, MD=mean diffusivity

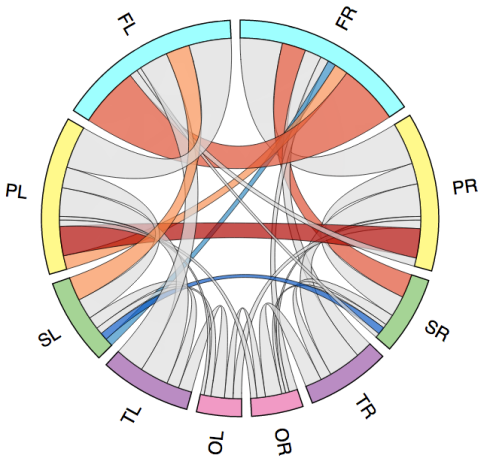

Figure 2: Significant effects with age in connectivity-based bundles. Red and blue indicate negative and positive correlation, respectively. Light gray connections had no significant effects, and more saturated colors indicate more numerous significant results. The population average bundle volume (sum of the fiber lengths) is mapped to chord thickness. Total bundle volume of each gray matter region is mapped proportionally to arc length. Key: L=left, R=right, F=frontal, T=temporal, P=parietal, O=occipital, S=subcortical