



Using White Matter Seed Regions Produces Stronger and More Complex Structural Networks in Healthy Elderly Subjects and Subjects with Alzheimer's Disease

and individuals with Alzheimer's disease.

Introduction

Whole-brain structural networks derived from MRI data are built from fiber tracts, which are generated using measurements of the orientation of water motion embedded in diffusion tensor imaging (DTI) or high angular resolution diffusion imaging (HARDI) data. These tracts need starting points, or seeds, and ending points, or targets. We investigated how using gray matter (GM) or white matter (WM) regions of interest (ROIs) as seeds impacts structural networks derived from DTI and HARDI data.



Figure 1: (top left) One subject's left superior parietal cortex GM ROI (red) and WM ROI (blue) and the primary diffusion direction in each voxel are shown overlaid on that subject's apparent diffusion coefficient (ADC) map. With an FA threshold of 0.1, many of the voxels within the GM ROI do not survive thresholding (empty red voxels). Most of the WM ROI voxels survived thresholding and the primary diffusion direction in these voxels is well-aligned with that of WM voxels deep to those in the WM ROI. (top right) The same subject's T1-weighted image of the left superior parietal cortex. (bottom) Rhesus macaque precentral gyrus stained with the pan-neuronal antibody SMI-311. The primary direction of neurites in the white matter (left) appears to be nearly orthogonal to the primary direction of neurites in the gray matter (right) in this section.

Figure 2: (left) DTI: One subject's fiber tracts generated between the left superior and inferior parietal cortex using a WM seed ROI (top) and GM seed ROI (bottom) (right) HARDI: One subject's fiber tracts generated between the left superior and inferior parietal cortex using a WM seed ROI (top) and a GM seed ROI (bottom)

Approximately double the number of fibers were generated between these two ROIs when initiating tracts from WM ROIs compared to GM ROIs.

Methods

Subjects: Ten healthy control subjects and ten subjects with probable AD were selected from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database, and HARDI data were acquired from five healthy control subjects and five subjects with probable AD participating in Boston University's Healthy Outreach Program for the Elderly (HOPE) study.

MRI: T1-weighted images and DTI datasets acquired on 3T GE scanners were selected from the ADNI database. DTI datasets were acquired with 41 directions, a b_{max} of 1000, and were resliced to isotropic voxels with dimensions 2.7 x 2.7 x 2.7 mm. T1-weighted images and HARDI datasets were acquired on the 3T Philips scanner at the Center for Biomedical Imaging at the Boston University School of Medicine. HARDI datasets were acquired with 64 directions, a b_{max} of 3000, and a resolution of 2 x 2 x 2 mm.

Generation of WM and GM ROIs: GM ROIs were defined using the Desikan-Killiany atlas in FreeSurfer. WM ROIs were defined as a strip of voxels located one voxel below the gray/white border of each GM ROI (See Figure 1).

Tractography and Network Construction

DTI: The diffusion data were reconstructed and fit to a tensor model using DSIstudio. Deterministic tractography was performed using DSIstudio to create a WM-seed network and a GM-seed network for each subject using the following parameters: FA Threshold = 0.1, Angle Threshold = 45°, step size = 2 mm, smoothing = 0.5, minimum fiber length = 5 mm, maximum fiber length = 300 mm, seed number = 10,000 per ROI, random subvoxel seeding, Gaussian radial interpolation, Runge-Kutta 4 (RK4) tractography algorithm. HARDI: The eddy_correct function in FSL was used to correct for distortion caused by eddy currents. The orientation distribution functions (ODFs) for each voxel were reconstructed in DSIstudio using GQI. The diffusion sampling length ratio was 1.25 and ODF sharpening was carried out using decomposition with a decomposition fraction of 0.04 and a maximum fiber population of 8. An 8-fold ODF tessellation was used to resolve 3 fibers per voxel. Deterministic tractography was performed using DSIstudio to create a WMseed network and a GM-seed network for each subject using the same parameters for DTI with a few changes: QA threshold = 0.07, step size = 1 mm, random subvoxel seeding using the primary diffusion direction, Gaussian radial interpolation, Runge-Kutta 4 (RK4) tractography algorithm. For both DTI and HARDI data, WM ROIs were used as seeds and GM ROIs as targets in WM-seed networks. In GM-seed networks, GM ROIs were used as seeds and targets. The number of fibers between a seed and target ROI were used as a measure of connection strength between the two regions (see Figure 2).

Network Comparisons: The Network Based Statistic (NBS) toolbox was used to perform within-group comparisons of WM-seed and GM-seed networks and between-group comparisons using either WM-seed or GM-seed networks using DTI and HARDI data to determine whether (1) weighted networks produced by WM and GM seeds differ within control or AD groups and (2) the results of between-group comparisons performed using WM-seed or GM-seed networks differ.

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eft precentral Left superior frontal Left superior parietal Left insula **Right inferior parietal Right lateral occipital** Right middle temporal Right precuneus Right superior frontal Right superior parietal **Right insula**

permutations = 5000

Node (Controls)

Right superior parietal

Right superior temporal

Right insula

Left inferior parietal Left rostral middle frontal Left superior parietal Left supramarginal Left insula Right fusiform Right inferior parietal Right precuneus Right superior parietal

Learning Objective: Compare the impact that seed region has on the construction of whole-brain structural networks generated from diffusion-based fiber tracking in healthy elderly individuals

ode ol > AD seed	Number of Differential Connections	Node Control > AD GM seed	Number of Differential Connections
	4	Left precentral	2
ngulate	5	Left rostral middle frontal	2
	5	Left temporal pole	2
IS	4	Left hippocampus	2
oarietal	5	Left thalamus	5

when using a DTI dataset and potentially when using a HARDI dataset.