Thresholding to Improve Estimation of Brain Stem Connectivity via Tractography

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Introduction

The brain stem is a highly complex region of the brain that contains areas that regulate the vital functions of the sleep-wake cycle, cardiac function, and respiratory function [1]. DWI and tractography provide an ideal tool to understand changes in the brain stem structure associated with neurological disorders [2] since DWI and tractography can provide a comprehensive look into the neural connections of the brain in vivo and with little risk to subject [3]. One of the biggest challenges facing current methods of tractography is false positives resulting from noise and low spatial resolution of in vivo measurements. Thresholding tractography maps to limit the amount of false positives in the data set may be extremely useful in the diagnosis of neurological diseases. The goal of the protocol was to optimize the acquisition sequence for the brain stem, which can to be performed in less than 20 minutes, without sacrificing the quality of the data. Then limit the number of false positive through the application of a threshold filtering of the calculated streamline tracks.

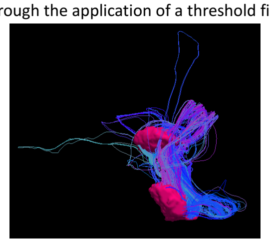

Figure 1. A depiction of the connectivity between two regions of the brain. Displayed is the fiber connectivity between the Thalamus and Pons.

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Hypothesis

We Hypothesize that:

- The use of thresholding to limit the number of false positive streamlines of tractography will yield a more accurate representation of the architecture of the brain stem.
- A more accurate view of the connectivity profile of streamlines throughout the brain stem will allow for the visualization of white matter specific regions of the brain ordinarily too small to see at clinical resolution.

Methods

Eleven healthy control participants, between the ages of 20 and 40 years, were recruited with no prior history of neurological disorders. Participants were scanned using a 3.0 T Phillips system with a 32-channel head coil. A high-angular-resolution diffusion imaging (HARDI) sequence was acquired. A total 71 directions were obtained; 1 with b = 0, 6 with b = 100 s/mm^2 and 64 with b = 1000 s/mm^2 using a model electrostatic repulsion to determine the diffusion gradient directions [4]. The acquired image resolution was 1.7 x 1.7 x 1.7 mm^3, TR/TE = 5000/86 ms, and Δ / δ = 42.1/9.1 ms. These images were then interpolated by a factor of 2 using cubic convolution with the CONGRID function in IDL for a final image resolution of 0.85 mm isotropic.

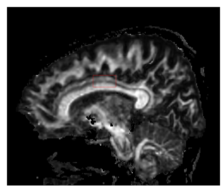

Figure 2: Sagittal view of the brain taken from FA space.

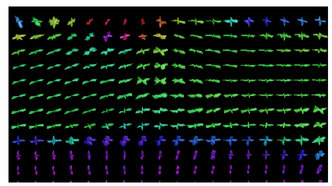

Figure 3:.MOW glyphs from the boxed region in Figure 2 reconstructed using a displacement probability function .

The fractional anisotropy (FA) and mean diffusivity (MD) maps were reconstructed from the HARDI data using in-house software written in IDL (Exelis Visual Information Systems, Boulder, CO). The thalamus and the pons were hand drawn using ITKSNAP with the FA and MD maps as references. The mixture of Wisharts (MOW) model was utilized for reconstruction of the fiber orientations [5]; this model characterizes a displacement probability function allowing the estimation of multiple fibers per voxel. MOW was calculated four separate times per data set each with a different probability displacement radius of: 13, 16, 18, and 20 microns.

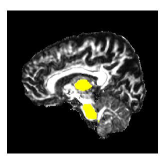

Figure 4. Highlighted regions represent the ROIs used in this study. The top is the Thalamus and bottom is the Pons

Utilizing the maxima of the displacement probability function as fiber orientations, deterministic tractography was performed with 125 seeds per voxel, fiber step size of one-half voxel, and no step-to-step angular deviations greater than 50°. The streamlines connecting the Pons and Thalamus ROIs were generated using in-house C based software. The streamlines connecting the 2 node-network (i.e. Pons and Thalamus) was converted into a tract density mask with each voxel containing an intensity value corresponding to the number of streamlines passing through that voxel. Finally a threshold was applied to the density maps for voxels containing less than 1%, 3%, 5%, and 10% of the maximum number of streamline tracts

Results

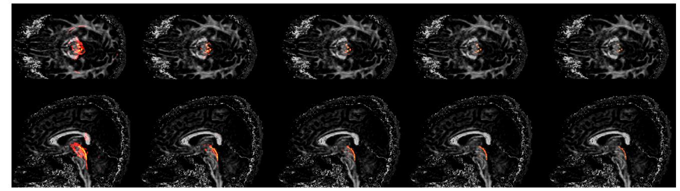

Figure 5. Density maps of connecting streamlines between the Pons and Thalamus. Top row transverse and bottom row sagittal views. Images from left to right: Increasing threshold from 0%, 1%, 3%, 5%, and 10% of the maximum number of streamlines where yellow voxels contain a large number of streamlines and red the least.

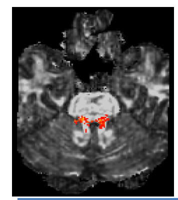

Figure 6. Transverse view in the Pons with yellow highlighted voxels believed to contain tracts that make up the Locus Coeruleus.

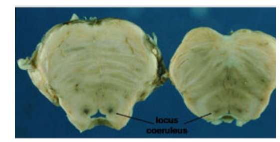

Figure 7. Excised Pons with staining in the Locus Coeruleus that could be used to validate the location of the Locus Coeruleus in MRI scans

Conclusions and Future Work

- Through the use of Tractography and thresholding, we were able to increase the visualization of our density maps allowing us to better look at areas of extreme streamline density compared to their surroundings.
- Future work will include changes to our tractography protocol, different forms of registration, and alternate ROIs used for tractography

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