Examining structure and function in a cognitive task

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Introduction

Recently, a great deal of research has focused upon investigating the relationship between the functional and structural networks that make up the brain. A popular approach is to use functional MRI (fMRI) to identify functionally activated regions of the cortex and diffusion tensor MRI (DT-MRI) to examine structural properties of the white matter pathways that connect the functionally identified regions [1]. This approach examines task-induced fluctuation in the blood oxygenation level-dependent (BOLD) signal. Specifically, the task involves a sentence completion paradigm where the subject is presented with two choices, one homophone and one alternative and is instructed to choose the word that reduces ambiguity. Canonical correlation analysis is used to examine the relationship between structure and function in language network.

Methods

To provide a common framework for analysis, the ANTS toolkit [2] is used to create a population specific-atlas from each subject's T1 and DT image. A mapping between this population atlas and MNI space is found to allow for comparison of T1, DT-MRI and fMRI in a common space. A population analysis of a language-based task identifies activated cortical regions of interest, and these regions are used to examine subject-specific activation levels. Additionally, these population regions are used along with tractography in the diffusion tensor component of the atlas to identify white matter pathways that provide the connections between these regions. Model pathways are determined and used to calculate average FA values for each pathway in each subject.

fMRI Analysis

Subjects were presented with both control and task items. Control items followed the same format of the experimental items but did not include a homophone. A total of 20 task items were presented. SPM5 is used to realign each image to the first image in the series and coregistered with the structural image [3]. The functional images are then transformed into MNI152 space and interpolated to isotropic 2mm voxels. A general linear model approach is used to calculate parameter estimates for each subject. A second level random effect analysis of these estimates allows for inferences across participants. Six regions of activation that survive a 20 voxel extent and cluster-level significance of $p < 0.05$ are identified. Here we limit the study to three regions found in the left hemisphere, illustrated in figure 1. For subject-specific activation values, these regions are used as masks. Each subjects' t-score map is examined to find the peak t-value in each region. The peak locations define the center of a 6mm sphere. All voxels within the sphere are averaged to determine an activation value for each region in each subject.

DT-MRI Analysis

The diffusion tensor component of the atlas is used to perform whole brain, deterministic fiber tractography with the Camino toolkit [3]. All voxels with an FA of 0.2 or higher are used as seed points for deterministic tractography. The tracking proceeds from each seed point with a fixed sub-voxel step size of 0.5 mm. The local streamline direction is computed by trilinear interpolation of the eight neighboring principal directions, and tracking continues until the local FA falls below 0.15 or the streamline curves by more than 60 degrees over the length of a voxel. The functional activation regions are dilated by 5mm to extend into the white matter and used as target regions to identify bundles of fibers that connect two regions of interest. For each region-to-region bundle of streamlines, each streamline is parametrized by arc-length to extend from 0.0 to 1.0. A BSpline is then fit to the set of all points from all streamlines in each bundle to obtain a single model pathway that lies in the core of the fiber pathway of interest. The model pathways are then warped into each subject's native DT-MRI space using the transform from the atlas building process and are used to calculate the average FA along each pathway. The model fiber pathways are illustrated in fig. 1.

Results

Canonical correlation analysis (CCA) was used to identify correlations between functional activation and structure using R [5]. Each of the three correlation coefficients provided by CCA has corresponding weights for each of the activation and FA values. In each case, taking activation weight of largest magnitude and FA weight of largest magnitude resulted in a pair containing a cortical region and a fiber pathway that connects to that region. The largest correlation implicated the orbital frontal cortex and the uncinate fasciculus, the second correlation implicated the medial temporal cortex and the extreme capsule, and the third correlation implicated the anterior temporal cortex and had similar weights for both the uncinate fasciculus and inferior longitudinal fasciculus. Permutation testing with 10K iterations was used to calculate a p-value for each correlation. All correlations and weights are listed in table 1.

	Activation Weights			FA Weights		
Correlation	Orbital frontal	Anterior temp.	Medial temp.	Uncinate	Extreme cap.	Inferior Long.
0.954 (p=0.5959)	-0.849	-0.094	-0.551	-14.625	-4.474	11.068
0.863 (p=0.0052)	-0.148	-0.639	1.274	-19.262	-33.524	-22.302
0.413 (p=0.0545)	0.548	1.186	-0.165	21.094	-6.311	21.034

Table 1. Correlation, p-value and weights from canonical correlation analysis

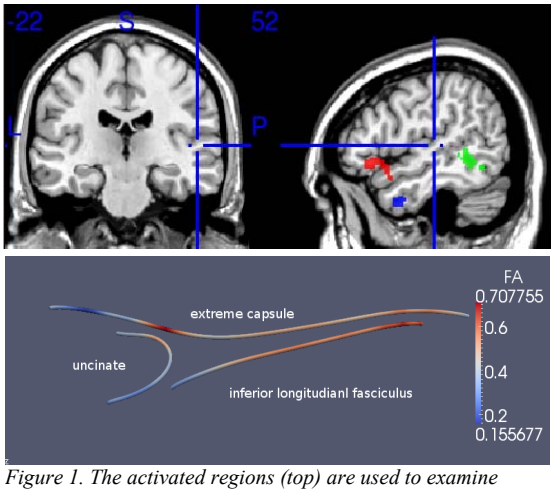

Figure 1. The activated regions (top) are used to examine function and also to identify the fiber tracts that connect them (bottom)

References
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