A White Matter Tractography Study of the Connectivity of Brodmann's Areas 4, 6 and 8

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Introduction

The aim of this study is to estimate the likely patterns of white matter connectivity to areas of the prefrontal cortex through the use of diffusion tensor MRI and white matter tractography. The cortical regions under investigation correspond to Brodmann's Areas (BA) 4, 6 and 8. Brodmann's Areas divide the cerebral cortex into regions based on cytoarchitectural features in a normalized space. The Brodmann regions appear to be related to specific brain function, and are used extensively to indicate specific brain locations in fMRI analyses. Previous studies have shown that fMRI response is constrained by anatomical connectivity [1]. Area 4, the primary motor area of the cerebral cortex, is located laterally on the precentral gyrus and medially on the paracentral lobule. Area 6, the supplementary motor area of the cerebral cortex, and Area 8, the pre-supplementary motor area, are located laterally on the precentral and middle frontal gyri, and medially on the superior frontal gyrus [2]. These cortical areas are important in motor and language function. A template, based on the Brodmann's Areas, was used to automate the selection of ROIs for the specific areas in this white matter tractography study. Consistent patterns of white matter connectivity for corresponding Brodmann's Areas were observed across sixteen healthy subjects.

Methods

DT-MRI studies were performed at 3-Tesla (b=1000s/mm^2, 12 encoding directions, voxel size = 2x2x3 mm). Eddy current distortion correction was performed using 2D affine coregistration in AIR [3]. B0 distortion correction was performed using a field map. Data was interpolated to 0.9375 mm isotropic dimensions. Three-dimensional maps of the DT and FA were calculated. White matter tractography was performed using as seed voxels all the brain voxels with FA values greater than 0.4. Fiber trajectories were generated using the streamline algorithm with a second-order Runge-Kutta integration method [4]. A Brodmann's area template (available with MRIcro software, Chris Rorden, www.mricro.com) was registered to each subjects FA data using a 3D affine image registration program (flirt from FSL; FMRIB, Oxford, UK; www.fmrib.ox.ac.uk/fsl/). The details of the method are presented elsewhere [5]. The regions of the template representing Brodmann's Areas 4, 6 and 8 were used to segment the tractography results. In each subject, trajectories were grouped according to the Brodmann's area in which they terminated. For each of the three Brodmann areas, the brain regions intersected by the associated trajectories were masked. Average masks of all the subjects, reflecting the between-subject probability of connectivity, were generated for each of the three areas under investigation. A probability threshold was applied to the average masks to remove potentially spurious voxels with low tract probabilities. To improve the correspondence between the tract masks from different subjects, the analysis was repeated with dilated individual masks (2 mm in this case).

Results

The white matter connectivity probability maps for BA 4, 6 and 8 are shown in Figures 1, 2 and 3 respectively. Regions of high tract probability are at the red end of the colorbar (dark red indicating all sixteen subjects had trajectories crossing a particular voxel). The tracts with probabilities less than 25% were removed. As can be seen BA 4 shows a strong connection in the corticospinal tract through the posterior limb of the internal capsule, and the basal ganglia and the corpus callosum. Tracts terminating at BA 6 show very strong patterns corresponding to tracts in the centrum semiovale and corona radiata, moving inferiorly through the internal capsule, and into the cerebral peduncles. BA 8 showed a similar pattern of connectivity with more anterior portions of the corona radiata. All three areas contained interhemispheric connections through the corpus callosum. A composite map displaying BA 4, 6 and 8 is shown in Figure 4. Voxels that contained tracts from more than one of the areas were assigned to the area with the highest average value.

Discussion

The use of a template based on Brodmann's areas in selecting ROIs for white matter tractography was found to be a promising method for mapping white matter connections for cortical areas associated with motor and language function. The tracts that were identified as connected with the particular areas appear to be consistent with known neuroanatomic pathways. The strong patterns of certain tracts in all three of the areas under investigation indicates consistent placement of the selection ROIs. Individual tractography results can be strongly influenced by image noise, partial voluming effects, and limitations of the tractography algorithm. However, the results show consistent patterns of connectivity across the sixteen subjects. These results demonstrate the promise of using Brodmann's Areas as a basis of selecting cortical regions for white matter tractography studies. Cortically specific white matter templates may be useful for quantitative ROI templates that could be used in group studies. Potential applications of WM templates for BA 4, 6, and 8 include the study of diseases that affect motor and language function such as MS, ALS, neoplasia and stroke.

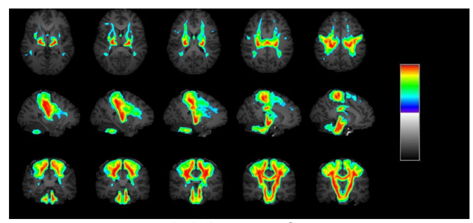

Figure 1: Tract probability map for BA 4.

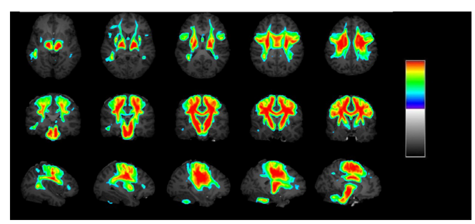

Figure 2: Tract probability map for BA 6.

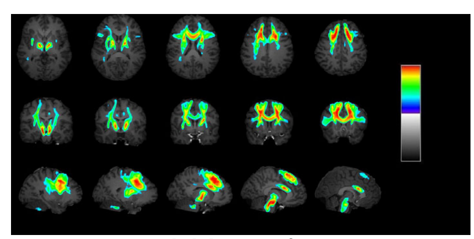

Figure 3: Tract probability map for BA 8.

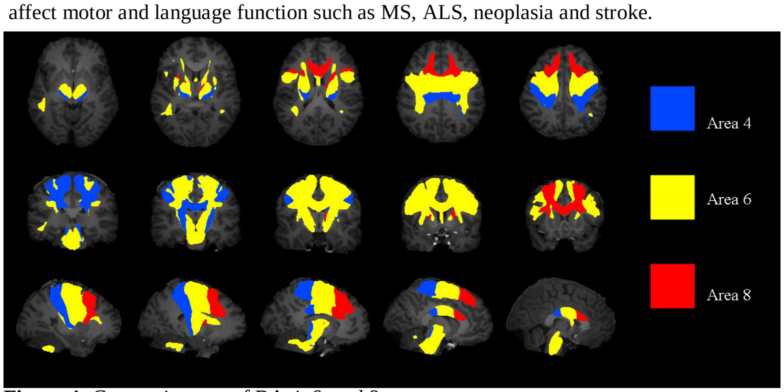

Figure 4: Composite map of BA 4, 6, and 8

References: [1]Toosy et al. NI 21:1452(2004) [2]Nolte, The Human Brain; 2002
[3] bishopw.loni.ucla.edu/AIR5/ [4] Lazar M et al. NI 2:1140 (2003)
[5] Thottakara et al., sub. to ISMRM 2004 [6]Ciccarelli et al. NI 19:1545 (2003)