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Diffusion Properties of Cortico-Striatal White Matter Tractography As Sensistive Markers of Parkinson's Disease

Y. Weldeselassie[1], G. Hamarneh[1], M. J. McKeown[2], S. Palmer[2], and M. S. Atkins[1]

[1]School of Computing Science, Simon Fraser University, Burnaby, BC, Canada, [2]Brain Research Centre, University of British Colombia, Vancouver, BC, Canada

Introduction

Diffusion Tensor Imaging (DTI) [1] is a non-invasive imaging modality that measures the local diffusion of water molecules through biological tissues. Recently, DTI fiber tractography has been employed for the analysis of several diseases [2-4]. Yoshikawa et al. demonstrate that patients with Parkinson's disease (PD) had significantly decreased fractional anisotropy in the region along a line between the substantia nigra and the lower part of the putamen/caudate complex, a region which includes the nigrostriatal dopaminergic pathway, a key site for degeneration in PD [3]. While the primary focus of neuro-degeneration in PD is the nigrostriatal pathway, neuroimaging studies have demonstrated widespread altered function within cortico-striatal-thalamo-cortical loops in PD [4]. In this paper, we investigate various properties of white matter fiber tracts connecting the primary motor cortex to the striatum from DTI in Control and PD subjects. After image acquisition, manual delineation of primary motor cortex and striatum, and generation of cortico-striatal fiber bundles, we collect features of interest and perform statistical analysis to see if such features can be used as markers in the classification of PD subjects from control subjects. In addition to the use of fractional anisotropy (FA) and mean diffusivity (MD), we investigated the divergence (DIV) of the major eigenvectors field of the DTI in the region of interest to assess any difference between the two groups. Our results show that PD subjects have reduced FA and MD but increased DIV of major eigenvectors field.

Materials and Methods

Seventeen subjects were considered in this pilot study. We recruited nine PD subjects, mean age 61±9 yrs, 4 female, 5 male, 8 right-handed, 1 left-handed. Patients were diagnosed with mild to moderate stage PD (Hoehn & Yahr stage 1 - 2.5). Data were compared to that from eight age-matched control subjects without neurological or psychiatric disorders, 4 female, 4 male, 7 right-handed, 1 left-handed. DTI were acquired using a Philips Achieva 3.0 Tesla scanner with slices parallel to the anterior commissure-posterior comissure line. 60 continuous slices of 2.2 mm thickness were collected with a field of view (FOV) of 212 mm, pixel size 0.82 mm^2. Three separate DTI scans were acquired for each subject and averaged during tensor reconstruction. CATNAP (http://iacl.ece.jhu.edu/~bennett/catnap/catnap.shtml) was used for rigidly aligning the three scans of each subject. Regions of interest (ROI) were manually drawn on a high resolution T1-weighted structural MRI, FOV 240 mm, pixel size $1mm^2$, with 170 continuous slices acquired parallel to the commissural line. The ROIs were transformed to the DTI frame of reference by registering the high resolution T1-weighted structural MRI to the FA map extracted from the DTI volume using AMIRA (http://www.amiravis.com). Fiber tracts were generated by seeding at the primary motor cortex with uniform density of one seed per voxel. Tracking was stopped when either the turning angle of fibers exceeds 45º or the diffusion approaches isotropic (FA < 0.25). As all fibers from cortex do not terminate at the striatum, only cortico-striatal fiber bundles were considered in our studies. Figure 1 shows cortico-striatal (red) together with cortico-spinal fiber bundle (blue). We extracted FA and MD values from every point in the DTI volume along the cortico-striatal fiber bundle. The divergence (DIV) of the major eigenvectors of the diffusion tensors along the cortico-striatal fiber bundle was also analyzed. Separate analyses were performed for FA, MD and DIV using unbalanced one-way analysis of variance (ANOVA) for comparing the means of control versus PD groups. We tested the null hypothesis that the mean values of the features extracted are drawn from the same population.

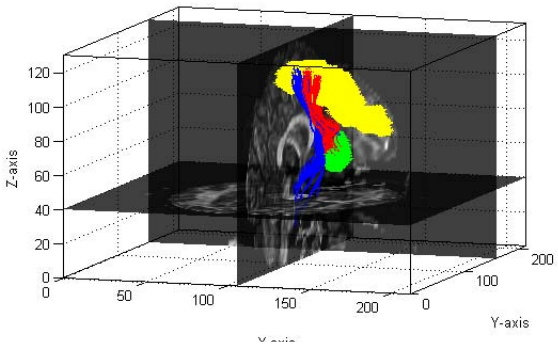

Figure 1: Motor cortex (yellow), Putamen (green) and Cortico-Striatal (red) and Cortico-Spinal (blue) fiber bundles.

Results

Reduced FA ($p < 0.06$) and reduced MD ($p < 0.03$) in PD were obtained compared to the normal controls. Moreover increased DIV ($p < 0.10$) in PD were obtained compared to the normal controls.

Discussion

The changes in FA and MD suggest that secondary changes in the cortex, far from the primary sites of pathology in PD, may be affected on the early stages of the disease, possibly as a compensatory mechanism. The increase in the DIV values of major eigenvectors among the PD patients may also provide another sensitive marker for PD, in addition to the often employed FA and MD features.

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